ORBITAL INTERACTIONS IN CYCLIC MOLECULES

A thesis
submitted in partial fulfilment for the
degree of
Doctor of Philosophy in Chemistry
in the
University of Canterbury, Christchurch,
New Zealand

by

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1988

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Abstract

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (oct-6-ene), 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (oct-6-ene) and exo-tricyclo[3.2.1.$0^{2,4}$]octane (oct-6-ene) with selected electrophiles are examined. Electrophilic attack at the cyclopropane ring occurs with inversion and this has been rationalised from a consideration of HOMO/LUMO interactions, and in particular, the secondary orbital interactions of the LUMO of the electrophile with the sigma framework in the HOMO.

Protonation of a cyclopropane occurs with substantial positive charge development in the transition state and this dictates that carbocation stabilities are qualitatively an important feature for understanding the reaction. For mercuration of a cyclopropane, the absence of significant charge development in the transition state is considered a consequence of poor overlap of the Hg 6s LUMO with the cyclopropyl HOMO orbitals and rearrangement is disfavoured. Where rearrangement is observed carbocation stability is important in dictating the reaction driving force.

When attack at either a similarly substituted double bond or cyclopropyl ring is possible, the regiochemistry of electrophile attack is rationalised from a consideration of cation stabilities. Proton attack occurs preferentially at a cyclopropyl ring while Br^+ attack occurs at a double bond. However, for mercuric acetate attack, there is no significant cation stabilising preference for attack at either a double bond or a cyclopropyl ring, and the regiochemistry of electrophile attack follows from a consideration of the relative contributions of the pi and cyclopropyl orbitals to the HOMO.

Chapter 1

A Bonding in cyclopropane

It has long been known that cyclopropanes react by undergoing addition[1] similar to the reactions of alkenes, while the higher alicyclics such as cyclopentane undergo reaction by substitution. This difference has been attributed to the strain which exists in the cyclopropane ring - cyclopropane having a strain energy of 27.5 kcal/mol as compared to 6.2 kcal/mol for cyclopentane.[2] However, while cyclopropane readily undergoes addition reactions with electrophiles, cyclobutane, with a similar strain energy of 26.5 kcal/mol is relatively unreactive.[2] For example, bicyclo[2.1.0]pentane is quite reactive towards bromine while bicyclo[2.2.0]hexane is essentially inert.[3]

In an effort to explain the bonding present in cyclopropane, theoretical models were developed by Walsh[4-6] (shown pictorially in Fig. 1)[7,8] and also by Coulson and Moffitt.[9] In the Walsh molecular orbitals of cyclopropane, the σ framework is made up of the $2a_1'$ and the degenerate 4e' orbitals. As only the $2a_1'$ orbital is bonding, the σ framework of cyclopropane is formally electron deficient. The π framework consists of the two degenerate bonding 3e' orbitals and the non-bonding $1a_2'$ orbital, and hence the π framework of cyclopropane is formally electron rich. Molecular orbital calculations (STO-3G) support an electron rich π system and an electron deficient σ system for cyclopropane.[8]

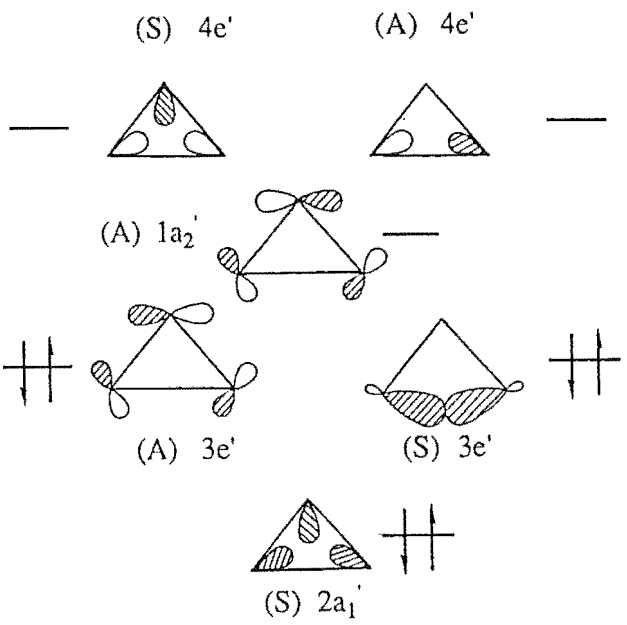


Figure 1

The Walsh molecular orbitals of cyclopropane.

The Walsh and Coulson and Moffitt models of cyclopropane, which have been shown to be equivalent[10], predict the presence of bent C-C σ bonds - a fact which has been experimentally verified[2] (Fig. 2).

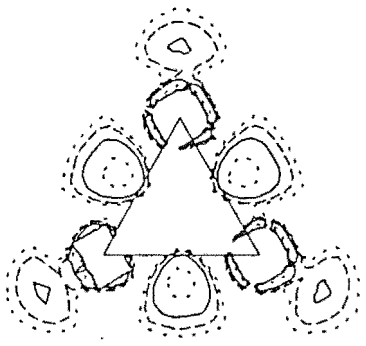


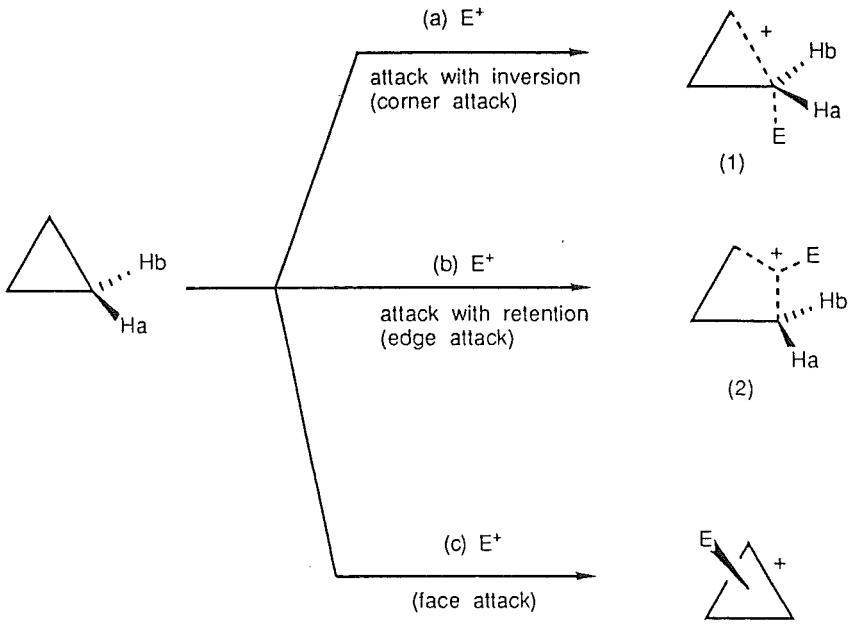
Figure 2 [2]

Electron density map of cyclopropane with the expected electron density due to three carbon nuclei at the three apexes subtracted.

Thus, the bonding in cyclopropane is different from the bonding present in "unstrained" alicyclics and its propensity to undergo addition reactions should no longer be considered anomalous.

B Electrophilic addition to cyclopropane

In the reaction of cyclopropane with electrophiles (E^+) (eg: Br^+ 11, H^+ 12, Pt^{2+} 13, Hg^{2+} 14 and various other metals[15]), three different reaction pathways are, in principle, possible (Scheme 1).



Scheme 1

The three possible modes of interaction of electrophiles with a cyclopropane ring.

Inherent in corner attack by the electrophile (path a) is inversion of configuration at the reacting centre, while edge attack (path b) results in retention of configuration. Theoretical calculations at all levels predict that for E = H, the face protonated cyclopropane (3a) is prohibitively less stable than the corresponding edge and corner protonated cyclopropanes (2a and 1a). However the same calculations yield conflicting conclusions as to the relative stabilities of edge and corner protonated cyclopropane - both species appearing to be energetically similar (Table 1).

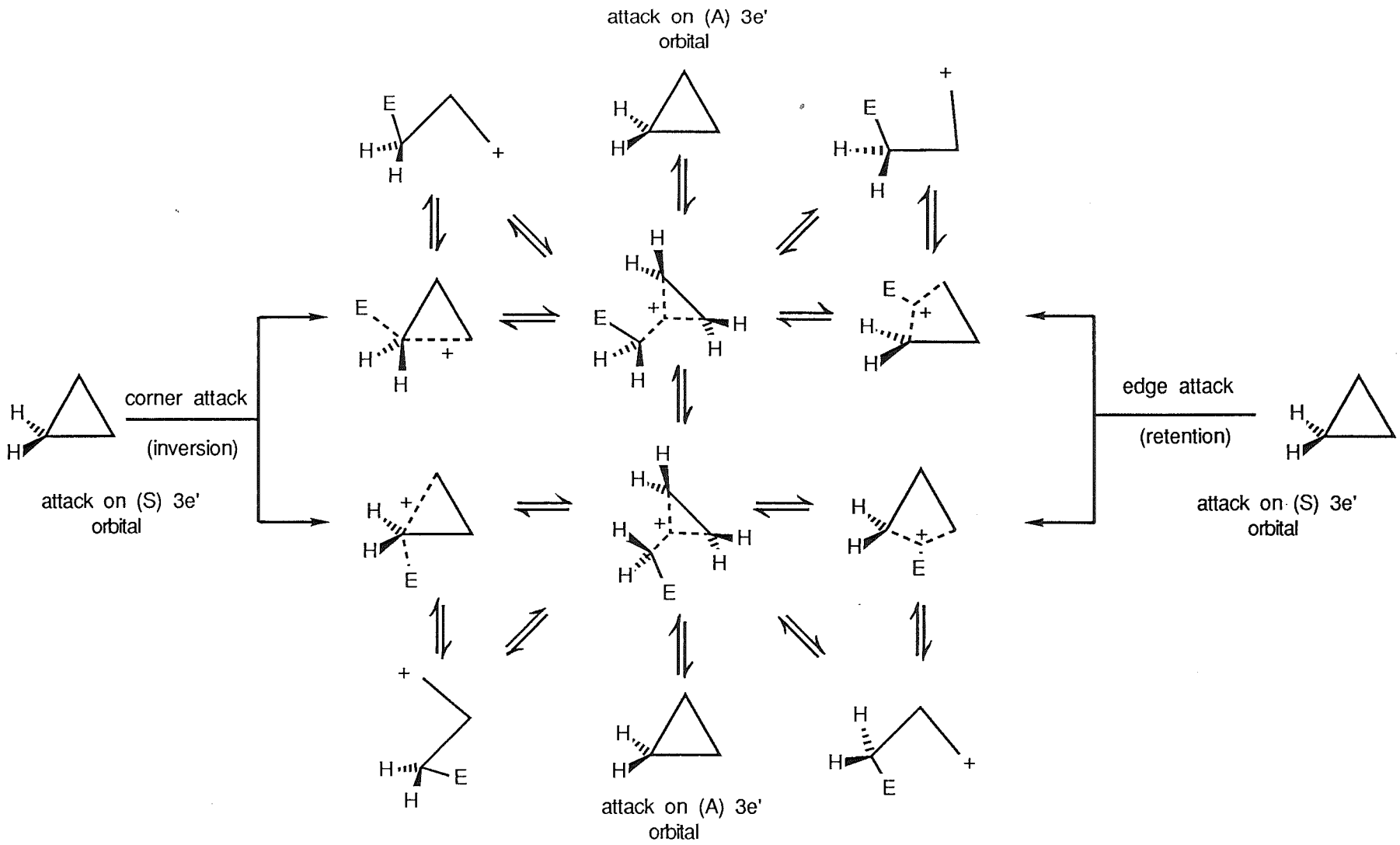
Table 1

Relative energies (Heats of Formation) of $C_3H_7^+$ isomers (kcal/ mol.) compared with 2-propyl cations.

	MP4(SDQ)[a] (16)	MP3[a] (3), (16)	MP2[a] (16)	HF/6-31G**[a] (16)	6-31G*[c] (17)	4-31G[18]	STO3G [18]	CEPA [19]	MINDO/2'[d] (20), (21)	MINDO/3[d] (22)
face (3a)					130.1	139.6	161.0	99.7	56.0	88.3
edge (2a)	(8.7)[b]	(7.8)[b] 8.1[e]	5.0	17.4	19.1	27.1	27.1	2.49	-3.9	7.5
corner (4)					13.1	17.4	22.9			
corner (5)	(8.2)[b]	(7.2)[b] 5.8[e]	4.7	13.7	13.0	17.3	22.8	7.52	3.5	12.3
1-propyl (6)					18.8	19.4	21.0	18.55		
1-propyl (7)	(19.7)[b]	(19.8)[b]	19.9	18.8	17.0	17.4	19.7	16.54	24.5	18.6
distorted 1-propyl (8)					14.1	16.9	20.5			
2-propyl (9)	0	0 3.9	0	0	0	0	0	0	0	0

See page 7 for the cation structures.

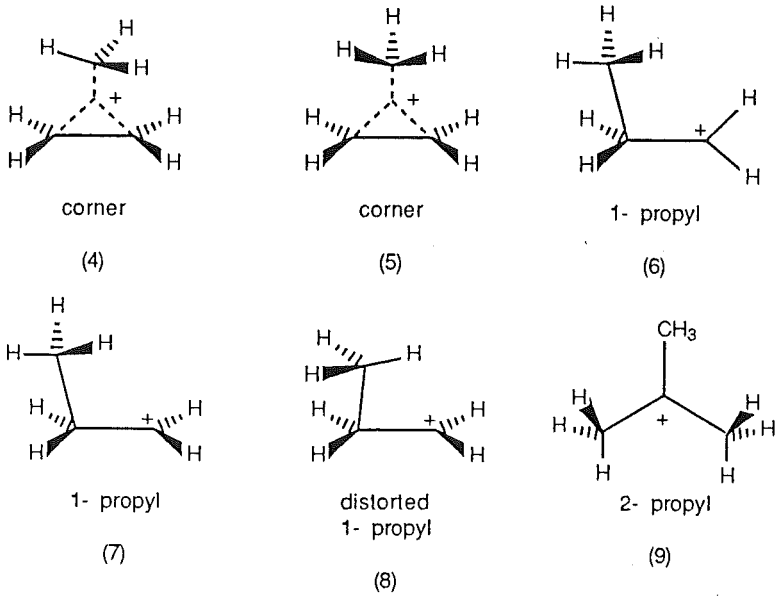
a 6-31G** basis and HF/ 6-31G* optimized geometries
b projected estimates based on the third and fourth order effects on the 6-31G* basis.
c includes d-functions on carbon.
d heats of formation.
e calculated values for cyclopropane + $CH_3OH_2^+ \longrightarrow$ edge or corner protonated cyclopropane. c.f. propene + $CH_3OH_2^+$, 3.9 kcal/mol.



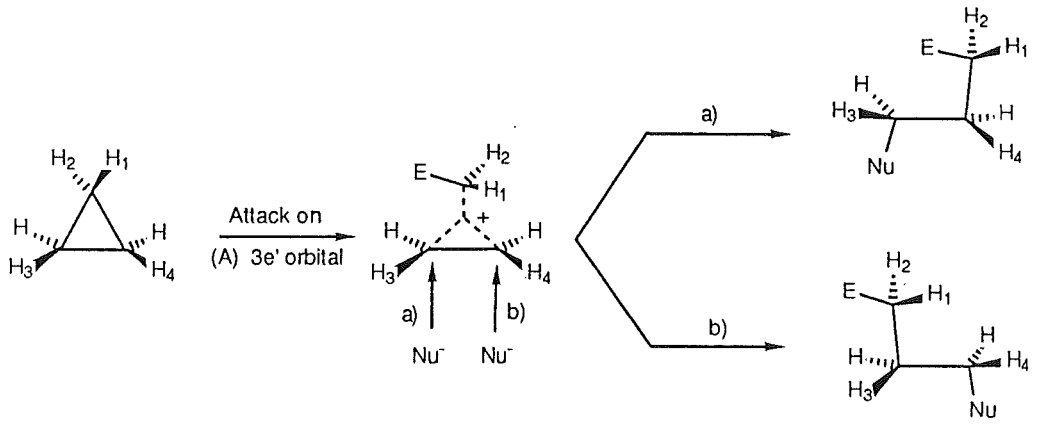
Scheme 2

Relationship between the $C_3H_7^+$ (E = H) cations.

Chemical evidence for the intermediacy of both edge and corner protonated cyclopropanes is well established - corner protonated cyclopropanes have been invoked to rationalise hydrogen and carbon scrambling in carbocations[23], and there is good evidence for the existence of edge protonated cyclopropane in the gas phase.[24]



Interconversion between edge and corner protonated cyclopropanes and the classical propyl cations is possible (Scheme 2) and therefore corner and edge attack by the electrophile should not be confused with the intermediacy of corner or edge protonated (E = H) cyclopropanes. Corner attack by electrophile on the (S) 3e' orbital of cyclopropane ultimately results in inversion of configuration at the reacting centre while edge attack on the same orbital yields retention of configuration by the electrophile. However, for electrophilic attack on the (A) 3e' orbital, either retention or inversion of configuration at the site of electrophilic attack may result depending upon which bond is broken (Scheme 3).



Scheme 3

For sufficiently dissymmetric cyclopropanes, it is possible to determine the mechanistic pathways involved in the reaction between an electrophile and cyclopropane. Experiments of this type have been undertaken and cyclopropanes have been found to undergo initial attack by the electrophile with subsequent nucleophilic attack with retention of both the electrophile and nucleophile[25], with inversion of the electrophile and nucleophile[26], and with inversion of nucleophile with both retention and inversion of electrophile[27]. Given this varied behaviour and limited data no explanation or generalisation has been advanced to rationalise the behaviour of substituted cyclopropanes with electrophiles.

C Reactivities of Cyclopropanes

(i) Protonation

Acid (or electrophile) promoted ring cleavage of cyclopropane generally follows a modified version of Markovnikov's rule which states[28] that the ring opening occurs

between the carbons bearing the largest and smallest number of alkyl substituents (Fig. 3).

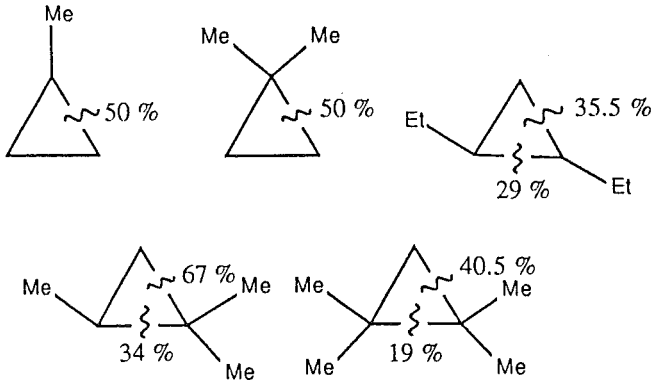


Figure 3

Bond cleavage in acid catalysed addition reaction

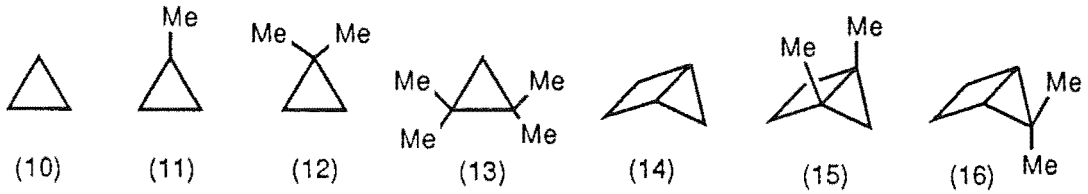
However, when substituents are on two carbons, products from cleavage of the more substituted cyclopropyl σ bond are also observed in addition to those that are to be expected by the above rule (Fig. 3).[3]

The reactivity of various substituted cyclopropanes with acid has been studied.[3,29] The rates of these reactions (Table 2) do not correlate with relief of strain energy as a plot of $\log k_{rel}$ *vs.* Δ strain energy reveals (Fig. 4)[29], thereby indicating strain relief is unimportant in determining cyclopropane reactivity. If interaction between the proton ls LUMO and the cyclopropane HOMO is an important feature of the reactivity of cyclopropanes, frontier molecular orbital theory[30] would predict a correlation between $\log k_{rel}$ and the first vertical ionisation potential (which is linearly proportional to the energy of the HOMO orbital). A fair correlation is found (Fig. 5)[29], but discrepancies still exist, especially for [3.2.1]propellane.

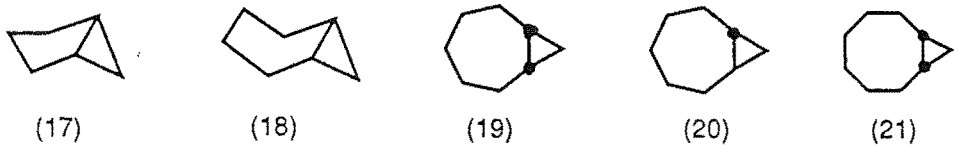
Table 2 [3]

Relative rates of acetolysis of substituted cyclopropanes.

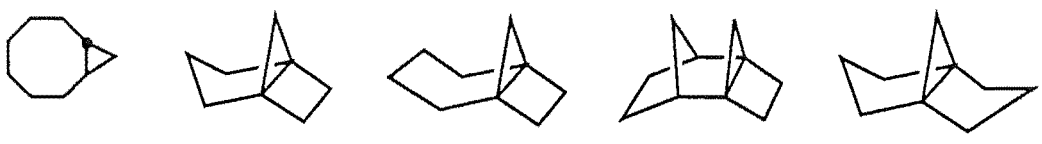
Compound		krel	log krel	Ionisation Potential (IP)	Strain Energy (Δ SE)
cyclopropane	(10)	4.9×10^{-5}	-4.3	10.9	28
methylcyclopropane	(11)	5.6×10^{-3}	-2.3	10.1	28
1,1-dimethylcyclopropane	(12)	0.065	-1.2	9.72	28
1,1,2,2-tetramethylcyclopropane	(13)	0.29	-0.54	9.18	28
bicyclo[2.1.0]pentane	(14)	1.0	0.00	9.55	51
1,4-dimethylbicyclopentane	(15)	2.0	0.30	8.8	51
5,5-dimethylbicyclopentane	(16)	79	1.9		28
bicyclo[3.1.0]hexane	(17)	0.011	-2.0	9.65	27
bicyclo[4.1.0]heptane	(18)	0.032	-1.5	9.46	27
cis-bicyclo[5.1.0]octane	(19)	0.017	-1.8		23
trans-bicyclo[5.1.0]octane	(20)	0.27	-0.57		33
cis-bicyclo[6.1.0]nonane	(21)	0.018	-1.7		24
trans-bicyclo[6.1.0]nonane	(22)	0.015	-1.8		25
[3.2.1]propellane	(23)	1.2×10^6	6.1	8.41	58
[4.2.1]propellane	(24)	93	2.0	8.50	48
tetracyclo[4.2.1^{2,5}.0^{1,6}] dodecane	(25)	1.9×10^6	6.3		
[3.3.1]propellane	(26)	0.36	-0.44		29



(10) (11) (12) (13) (14) (15) (16)



(17) (18) (19) (20) (21)



(22) (23) (24) (25) (26)

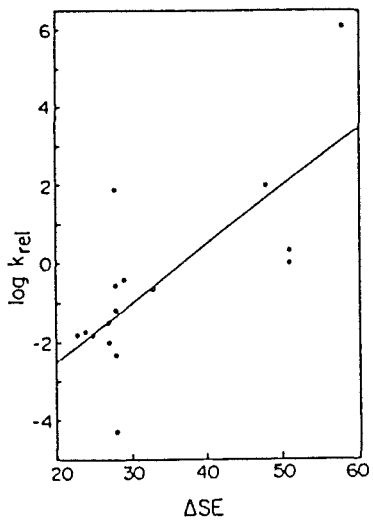


Figure 4 [29]

Relationship between the logarithms of the relative rates of acetolysis and the strain energy relief in the reaction. The correlation coefficient is only 0.75.

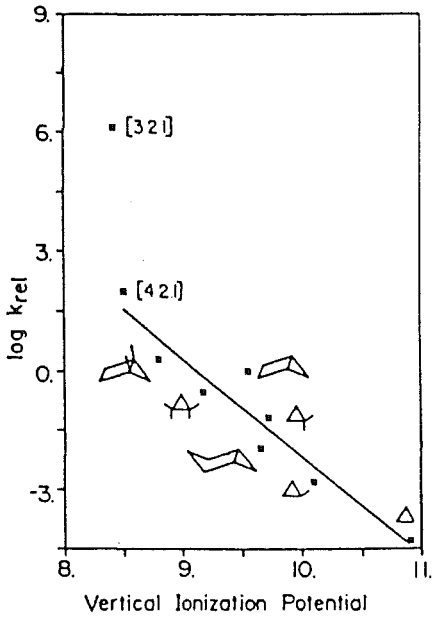


Figure 5 [29]

Relationship between the logarithms of the relative rates of acetolysis and the first vertical ionisation potentials of the cyclopropanes.

The reactions are thought to involve rate determining proton transfer at a rate which depends on the ease of polarisation of one (or more) of the carbon-carbon bonds, as represented by the calculated total electron population on a per molecular orbital

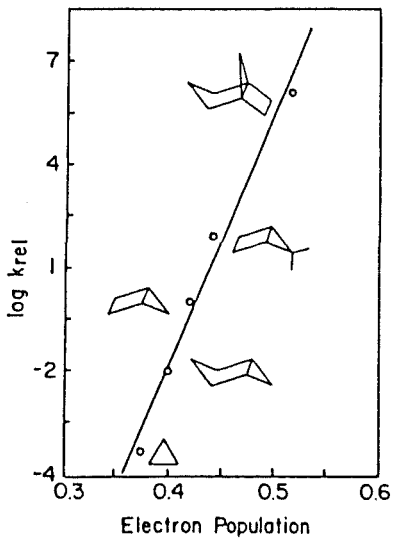
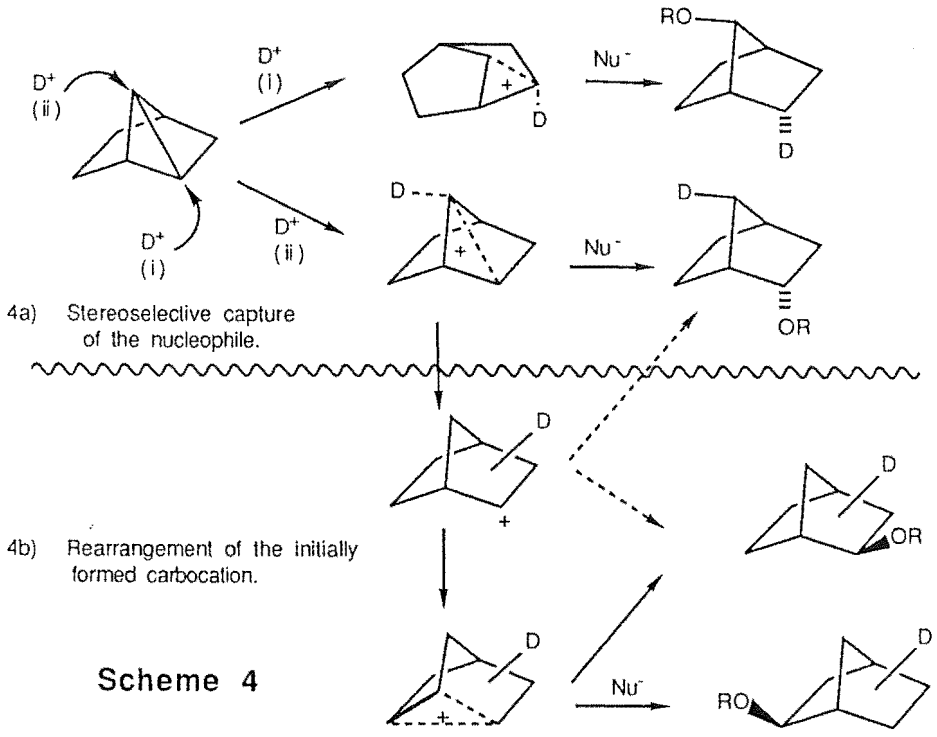


Figure 6 [29]

Relationship between the logarithms of relative rates of acetolysis of various cyclopropanes and the calculated electron population at the attacking proton 2 Å away from a ring carbon.

basis (Fig. 6).[29] As only approximately 50 % of the calculated electron density comes from the highest occupied molecular orbital[29], it is understandable why frontier molecular orbital theory yields only a rough correlation with the rates of acetolysis. The correlation found in Figure 6 indicates polarisation is one of the more important factors determining cyclopropane reactivity. Since relief of steric strain does not correlate with reaction rate, the transition structure is considered to be reactant like. The products are considered be formed by capture of the protonated cyclopropane before it has become an open carbocation, consistent with stereoselective capture by nucleophile (Scheme 4a). Rearrangement of the initially formed protonated cyclopropane may in some instances be competitive with nucleophilic capture[31] (Scheme 4b), thereby further complicating analysis of the reaction pathway.



Scheme 4

(ii) Mercuration

In contrast to the acid induced cleavage of cyclopropane, the stereochemistry of oxymercuration of cyclopropanes has been considered to be controlled by steric factors.[34] In a study of the rates of mercuration of various substituted cyclopropanes[32,33] it was found that 1,1-diphenyl-, 1,2-diphenyl- (both cis- and trans-), ethyl- and isopropyl-cyclopropane were all found to have approximately the same reactivity under standard conditions. Steric effects were considered to offset any subsequent gain in carbocation stability arising from further alkyl substitution. Additional methyl substitution increases the rate only slightly (Table 3).

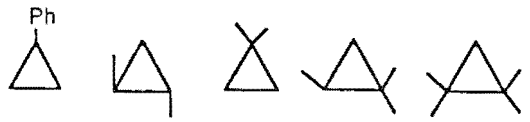
Compound	
Relative Reactivities.	1.0 1.1 2.0 2.2 2.5

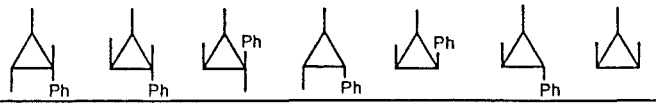
Table 3

Relative reactivities of substituted cyclopropanes to mercuric acetate (as indicated by the relative ratio's of the amount reacted under standard conditions - MeOH, $Hg(OAc)_2$, 20°C)

Further evidence for the importance of steric constraints in the oxymercuration of cyclopropanes has been found in a study of the mercuration of various phenyl- di- and tri-methylcyclopropanes[34] (Table 4). In the reaction of these compounds, the developing positive charge is best stabilised by the phenyl group, thus inducing C1,2 and/or C1,3 bond cleavage (Scheme 5). For 1-r-phenyl-1,2-trans-3-trans-trimethyl-cyclopropane (27), steric accessibility to the

Table 4

Stereochemistry of cyclopropane ring opening with mercuric acetates.

Compound							
Hg^{2+} retn : inv	0 : 100	0 : 100	0 : 100	88 : 12	18 : 82	28 : 72	38 : 62
CH_3OH retn : inv	0 : 100	0 : 100	0 : 100	10 : 90	9 : 91	25 : 75	0 : 100

cyclopropane was considered to be greatest along the C2,3 bond, thus requiring inversion of configuration by the electrophile However, with 1-r-phenyl-2-cis-3-trans-dimethylcyclopropane (28), attack along the C1,2 bond with the substituents being cis* is sterically favoured to attack on the 1,3 bond where the substituents are trans and gives rise to a predominance of retention by the electrophile at C2.

In a similar study of the mercuric acetate cleavage of phenyl-substituted cyclopropanes, a Hammett reaction constant $\rho = -3.2$ was observed, indicating the presence of substantial positive charge in the transition structure.[36] This is analogous to the oxymercuration of alkenes in water, where a Taft reaction constant $\rho^* = -3.3$ was found.[37] The lack of rearrangement in the oxymercuration of alkenes is often ascribed to an absence of substantial charge development at the reacting centre.[38] This is a consequence of extensive delocalisation of charge in the transition structure. The ability of the electrophile to stabilise an adjacent or proximate carbocation will, however, be of importance in preventing rearrangements.[39] The electrophilic species in

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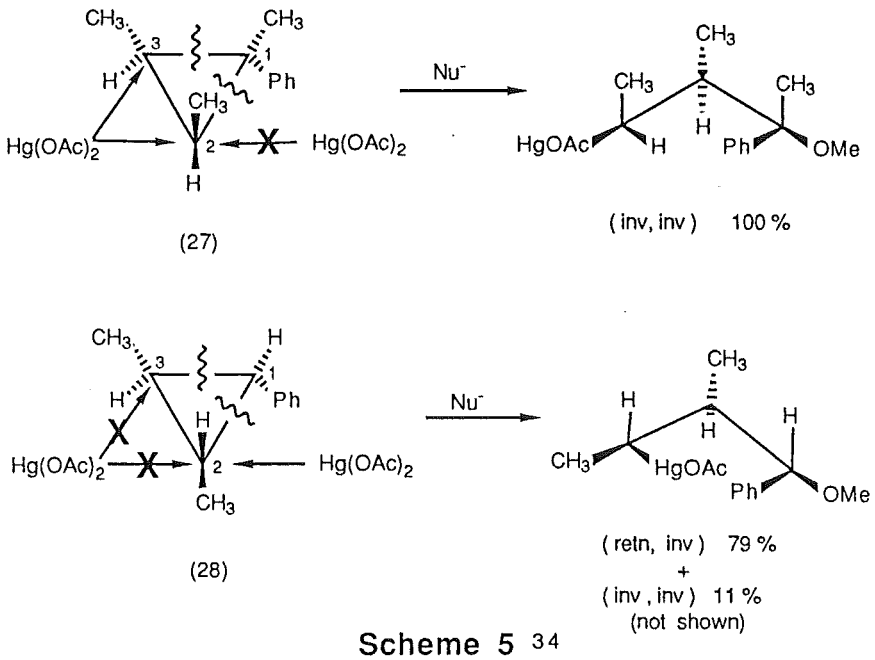
*Footnote: Alkene reactivity generally follows the trend 1-alkenes > 2-alkenes (cis > trans) > trisubstituted-alkenes.[35]



Scheme 5 [34]

Steric control of reaction course in the oxymercuration of phenyl methyl cyclopropanes.

these reactions was considered to be undissociated $Hg(OAc)_2$ or a related ion pair, and not $Hg(OAc)^+$. If $Hg(OAc)^+$, $Hg(OAc)_3^-$, or $Hg(OAc)_4^{2-}$ were the reacting species then it would be expected that, by the mass law effect, the rate upon addition of lithium acetate would decrease the concentration of $Hg(OAc)^+$, and increase the concentration of $Hg(OAc)_3^-$ and $Hg(OAc)_4^{2-}$, thereby affecting the rate of reaction dependent upon which of these species is involved. However, in the reactions of substituted phenylcyclopropanes with mercuric acetate in acetic acid[36], the effect of added lithium acetate on the reaction rate was unimportant, consistent with the electrophilic species in these reactions being $Hg(OAc)_2$ or a related ion pair, and not $Hg(OAc)^+$, $Hg(OAc)_3^-$ or $Hg(OAc)_4^-$.

The stereochemistry of attack of the nucleophile in the oxymercuration of 1-phenylbicyclo[4.1.0]heptane has been found to be dependent upon both the solvent and the mercuric salt used.[40] Observation of the syn to anti ratio (retention : inversion by the nucleophile) after lithium aluminium hydride

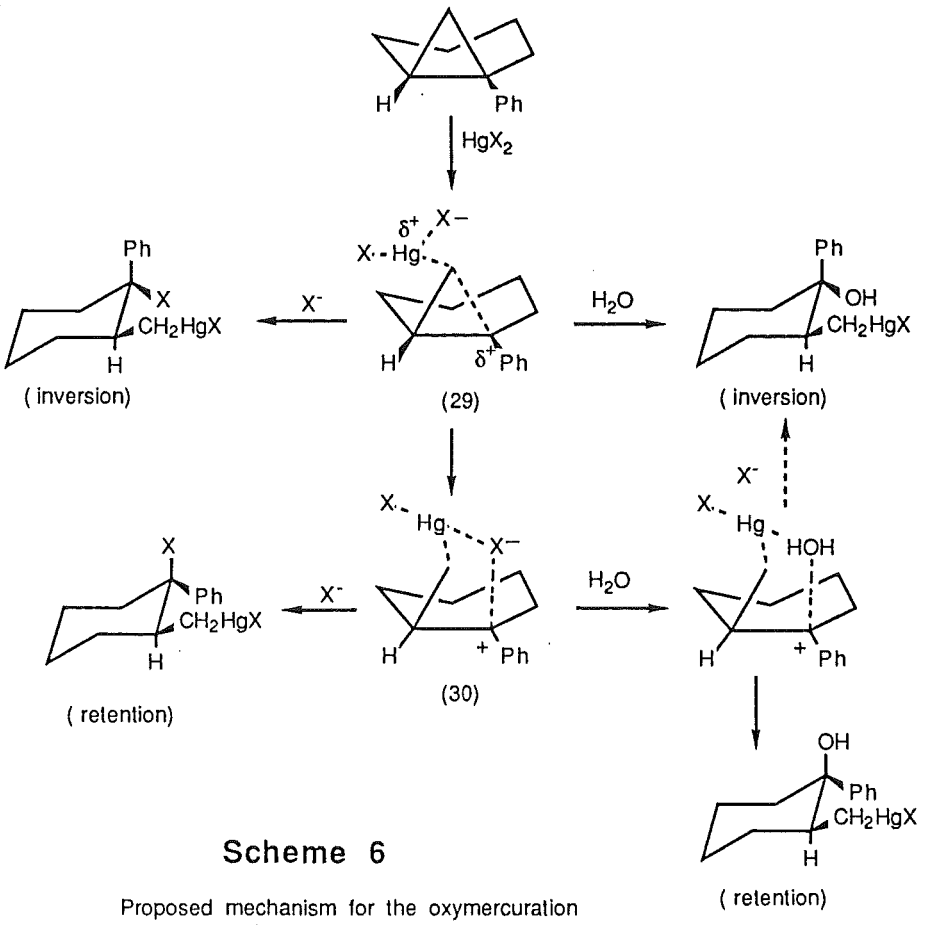
reduction of the organomercurial mixture gave the following results (Table 5). In non-nucleophilic media, the syn to anti

mercuric salt	solvent	Nucleophile retention : inversion (syn : anti product)
$Hg(OAc)_2$	H_2O	13.5 : 86.5
$Hg(O_2CCF_3)_2$	H_2O	19.5 : 80.5
$HgSO_4$	H_2O	22.5 : 77.5
$Hg(NO_3)_2$	H_2O	22.5 : 77.5
$Hg(ClO_4)_2$	H_2O	23.0 : 77.0
$Hg(O_2CCF_3)_2$	CCl_4	62.0 : 38.0
$Hg(O_2CCF_3)_2$	cyclohexane	69.5 : 30.5
$Hg(O_2CCF_3)_2$	benzene	71.0 : 29.0
$Hg(O_2CCF_3)_2$	CH_3NO_2	72.0 : 28.0
$Hg(O_2CCF_3)_2$	CH_2Cl_2	75.0 : 25.0
$Hg(O_2CCF_3)_2$	$CHCl_3$	82.5 : 17.5

Table 5 [40]

Stereochemistry of the nucleophilic step in the mercuration of 1-phenylbicyclo[4.1.0]heptane.

ratio increases with increasing solvent polarity, consistent with greater stability of the ion pair (30). A similar dependence of the stereochemistry of nucleophilic attack upon the solvent (and mercuric salt employed) has been observed in the oxymercuration of bicyclo[2.2.2]oct-2-ene.[41] Increasing polarity of the attacking mercuric salt ie: in going from $Hg(OAc)_2$ to $Hg(ClO_4)_2$, similarly gives rise to a larger syn : anti ratio. This is consistent with greater charge development in the intermediate thereby favouring (30), which ultimately yields syn product (Scheme 6). Incomplete bond cleavage in intermediate (29) favours attack with inversion by the nucleophile to yield product with an anti configuration. With the use of protic solvents in the reaction, nucleophilic attack by solvent is competitive with attack by X^-, the ratio of the two depending upon, among other factors, their relative nucleophilicities.



Scheme 6

Proposed mechanism for the oxymercuration of 1-phenylbicyclo[4.1.0]heptane.

(iii) Bromination

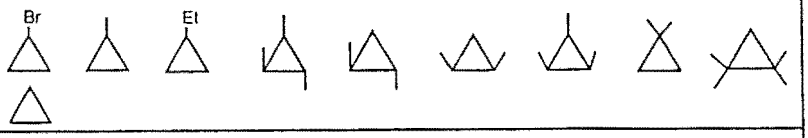
In contrast to the ease of attack of cyclopropanes by acid, bromine reacts only sluggishly with cyclopropanes in the absence of light.[42] In the presence of light, free radical processes dominate, leading to HBr formation and subsequent attack by proton. This is in contrast to the reactivity of alkenes, where bromine reaction is more rapid than reaction with acid.

Steric effects do not seem to inhibit reaction as in the mercuric acetate reactions, as is shown by comparison of the relative rates listed in Table 6[42] with those of mercuric acetate as shown in Table 3. For bromination, alkyl substitution results in a greater effect on rate than that

observed in acid catalysed acetolysis (Table 7), consistent with greater charge development in the intermediate(s) in bromination.

Table 6

Bromination of alkylcyclopropanes
(Br_2 - NBS, dark, 25°, CH_2Cl_2 solvent)

Compound									
k_{rel}	~0	~1.0	1.0	4.3	10.8	20.8	23.8	~100	>1000
K_{abs} ($l\ M^{-1}$)		$\sim 4.9 \times 10^{-4}$	4.9×10^{-4}	2.1×10^{-3}	5.2×10^{-3}	1.0×10^{-2}	1.2×10^{-2}	$\sim 4.9 \times 10^{-2}$	> 0.49

The extent of rearrangement observed in bromination of alkylcyclopropanes (Scheme 7) and the lack of stereospecifity in nucleophilic attack (Scheme 8) is consistent with the involvement of a substantial localised positive charge. However, it should be noted that an unsymmetrical corner brominated cyclopropane intermediate is required to accommodate

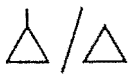
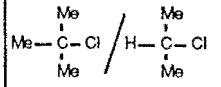
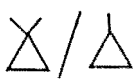
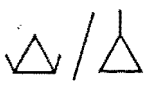
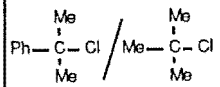
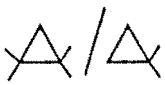
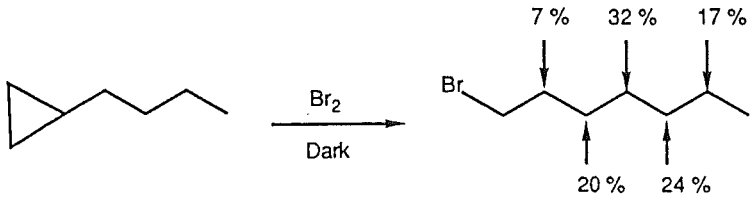
Compounds	Acid catalysed acetolysis (100°C) [3]	Bromination (25°C) [42]	Solvolysis of substituted isopropyl chlorides (80% EtOH/ H_2O, 25°C) [43]
	91	Large	 55000
	7	100	
	1	20.8	 4580
	3.3	ca. 10	

Table 7

Comparison of the effects of alkyl substitution on the relative rates of a) cyclopropane addition b) solvolysis.

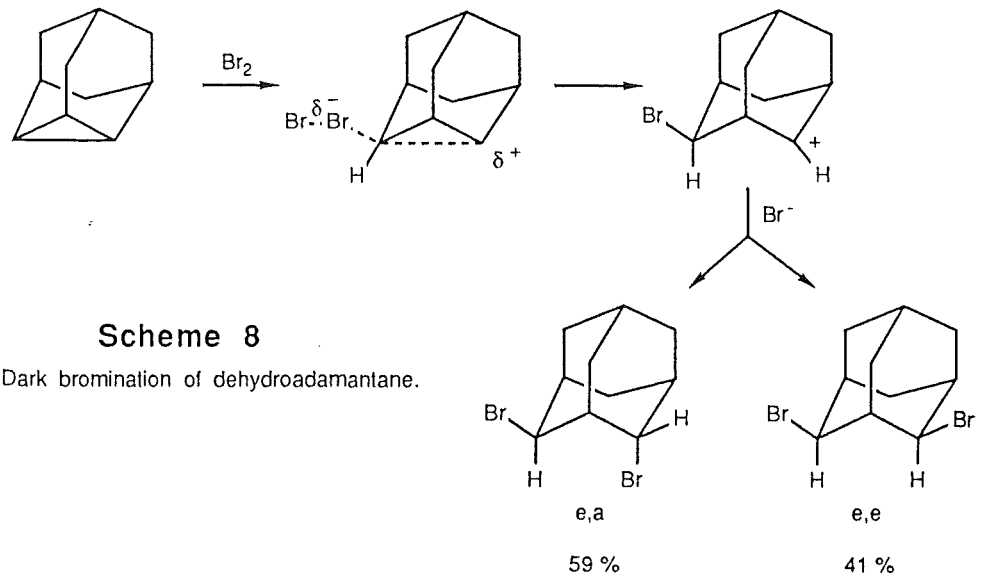
the results from the bromination of trans-1,1,2,3-tetradeuterocyclopropane.[11]



Scheme 7

Rearrangement products observed in the bromination of n-butylcyclopropane as indicated by the positions of Br^- attack.

Such an observation is consistent with the initially formed brominated cyclopropane, resulting from reaction with a substituted cyclopropane, readily rearranging to the classical analogue. For the corner brominated trans-1,1,2,3-tetradeuterocyclopropane there is no energetically favourable rearrangement mechanism since the classical cation, if it were formed, would be primary. It is of interest to note that the dark bromination of dehydroadamantane has been reported to give products resulting from attack with inversion by electrophilic bromine (Scheme 8).[42]

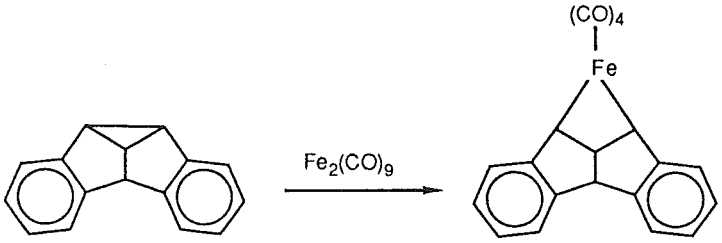


Scheme 8

Dark bromination of dehydroadamantane.

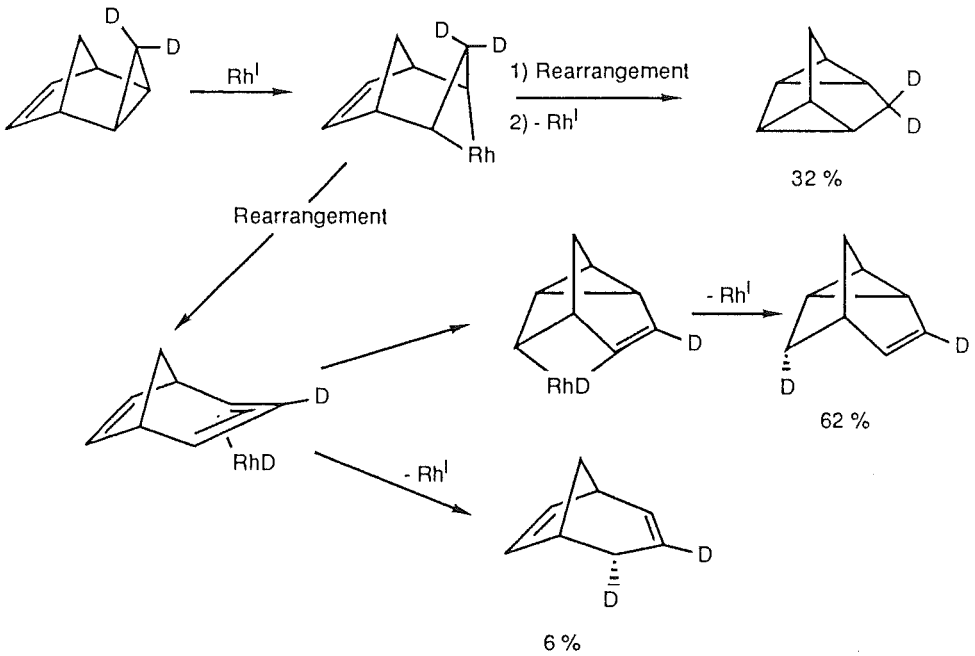
(iv) Platinacyclobutane formation

Cyclopropanes react with various metal ions and may form isolable organometallics[44] (Scheme 9) or give elimination products[45] (Scheme 10).



Scheme 9

Reaction of dibenzosemibullvalene with diiron nonacarbonyl.



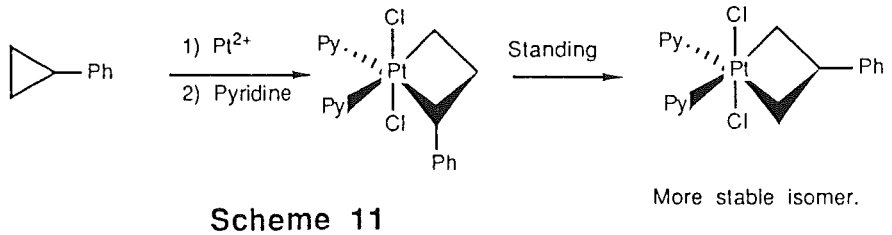
Scheme 10

Reaction of 3,3-dideutero-exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with $Rh(PPh_3)_3Cl$.

The reaction of Zeise's dimer ($[PtCl_2(C_2H_4)]$) with cyclopropanes is probably the most studied.[46] The cyclopropane reacts to form isolable tetrameric platinacyclobutanes, which usually regenerate the stereochemically pure cyclopropane

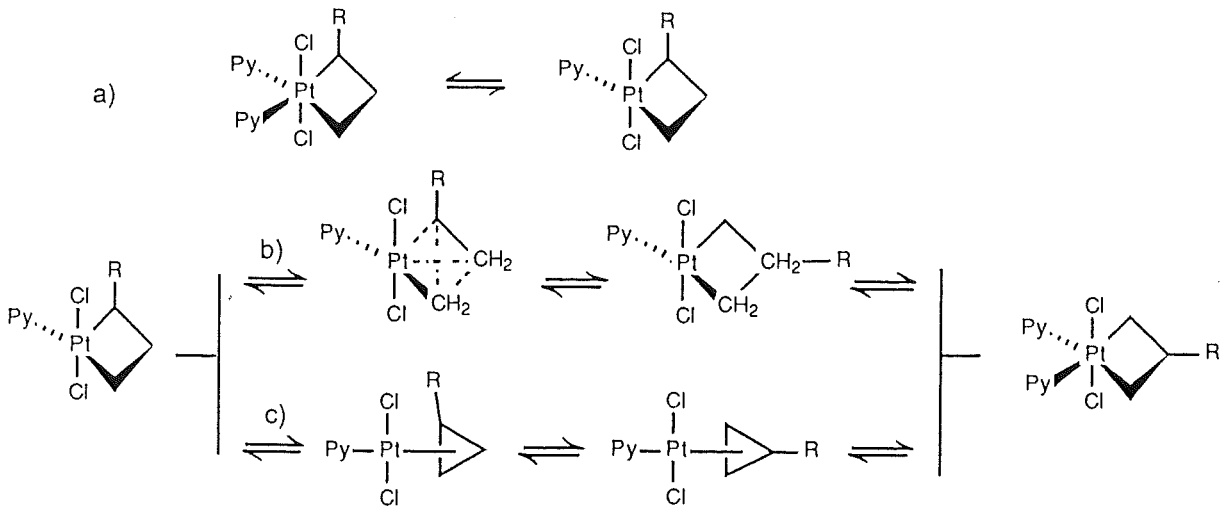
precursor upon treatment with CN^- or $P(Ph)_3$. The observation of predominant retention of stereochemistry in the regenerated cyclopropane has been taken to be evidence for concerted elimination of an edge complex of the cyclopropane with platinum.[46] Alternatively, a readily soluble monomeric platinacyclobutane can be prepared by treatment of the tetramer with pyridine or dioxane.

The role steric effects play in the formation of platinacyclobutanes is uncertain, as an initially formed compound may rapidly rearrange to a thermodynamically more stable isomer[47] (eg. Scheme 11). Such isomerisations proceed with retention of stereochemistry at the cyclopropyl substituents.[46]



Scheme 11

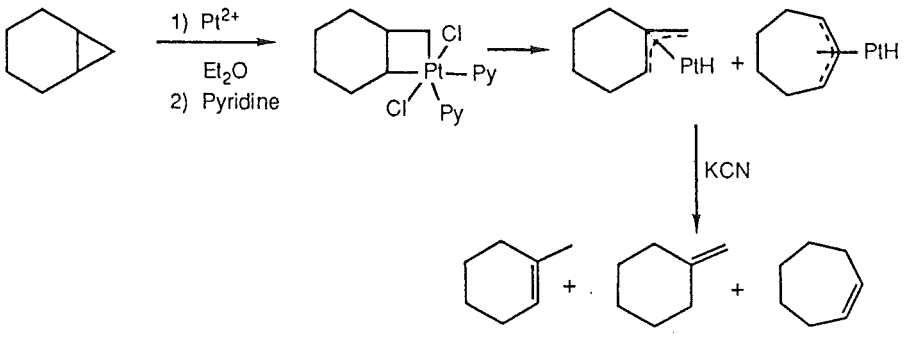
Isomerisation of platinacyclobutanes.



Scheme 12

Proposed mechanisms for the isomerisation of platinacyclobutanes.

The observation that the isomerisations are severely retarded in excess pyridine[47] implies loss of ligand as the first step (Scheme 12a). Two mechanisms consistent with these requirements have been proposed: (Scheme 12 b)[47, 48a] and (Scheme 12 c).[48] Rearrangement of the platinacyclobutane to form a π-allylplatinum complex may also occur[49] (Scheme 13).



Scheme 13

Rearrangement of platinacyclobutane to π allylplatinum complexes.

While the role of steric effects in the formation of platinacyclobutanes is unknown, electronic effects appear to be significant. Retention of the stereochemistry at the two reacting carbon centres in the formation of platinacyclobutanes

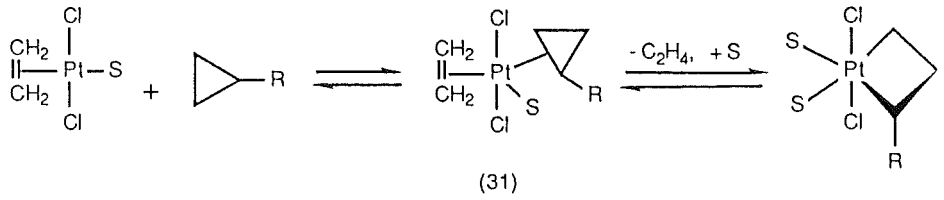
Ar	10^3 [aryl cyclopropane] (M)	10^4 kobs (s^{-1})	E_a (kcal mol^{-1})	$\Delta S^{\neq}$ (cal K^{-1} mol^{-1})
p-EtO Ph	4.09 34.0	62.9 243	15.6	-14.3
p-Me Ph	3.52 32.6	10.9 46.6	15.8	-12.9
Ph	3.82 36.4	3.55 20.7	15.7	-14.1

Table 8 [50]

Kinetic data for the reaction of arylcyclopropane + $[PtCl_2\ C_2H_4\ (THF)]$ at 318 K in THF. The reaction observes first order kinetics in both [arylcyclopropane] and $[Pt\ Cl_2C_2H_4\ (THF)]$.

precludes the formation of a fully developed carbocation with the accompanying loss of stereochemistry. However, the observation of increasing rate of platinacyclobutane formation with increasing solvent polarity[50] and also with the addition of electron releasing groups[50,51] (Table 8) on the reacting cyclopropane indicates polarity in the intermediate is important. Electron transfer or electron availability may also be of importance in these reactions.

A mechanism for the formation of platinacyclobutanes has been proposed[50] (Scheme 14), consistent with the requirement of an associative process indicated by the large negative entropy of activation in Table 8. This mechanism involves formation of an edge complex (31) and subsequent ring opening to yield the platinacyclobutane. It is not known which step is rate determining, but by comparison with the other electrophilic additions to cyclopropane it would be expected that the first step be rate determining.



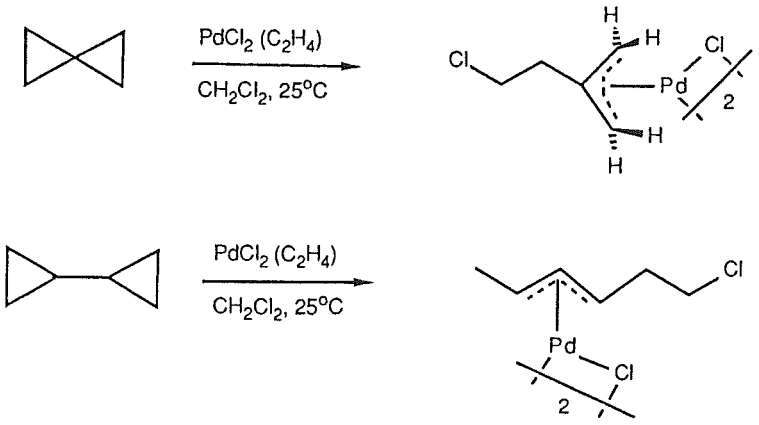
(31)

Scheme 14

Proposed mechanism for the formation of platinacyclobutanes.

(v) Chloropalladation

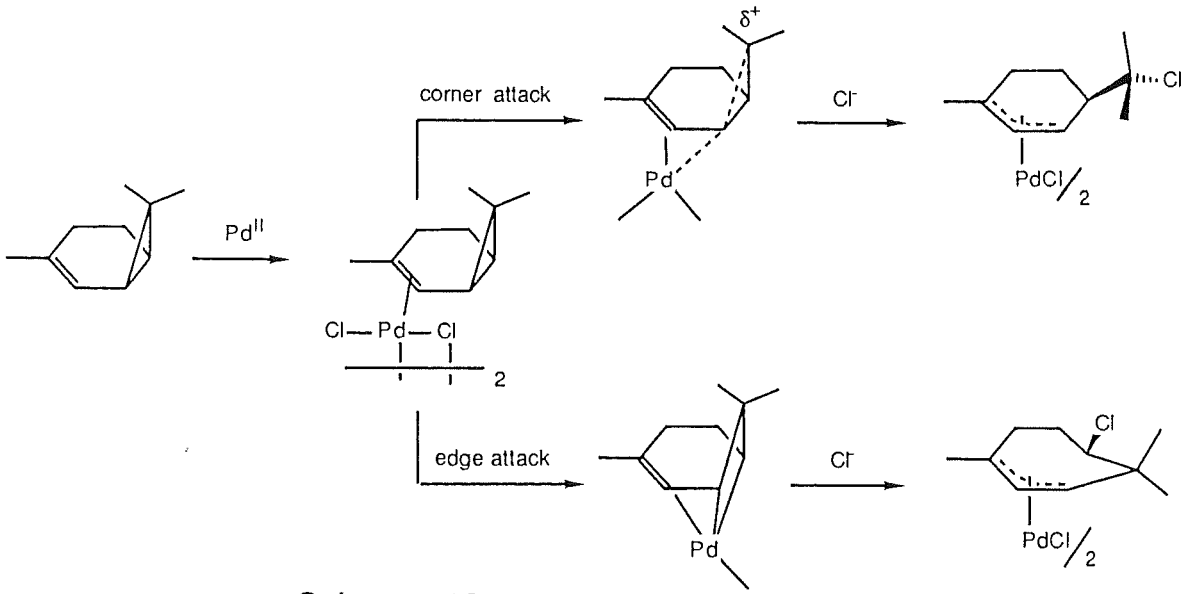
In a similar manner to platinum(II) addition to cyclopropanes, addition of a palladium(II) chloride may yield a π-allyl compound (Scheme 15)[52,53] via a chloropalladation reaction.[54] However, unlike platinum(II) where addition has



Scheme 15

π -allyl palladium formation.

been found to occur exclusively along the edge of the cyclopropane ring, the palladium(II) attack on cyclopropanes has been found to occur by edge attack, corresponding to the formation of a palladacyclobutane by oxidative addition, by corner attack or by a mixture of the two. This latter situation is found in the chloropalladation of (+)-2-carene (Scheme 16).[55] The direction of palladium(II) attack



Scheme 16

Corner attack and edge attack by palladium (II) on (+)-2-carene.

was found to be strongly dependent upon the solvent employed - the ratio of corner to edge attack being 1:6.1 in benzene,

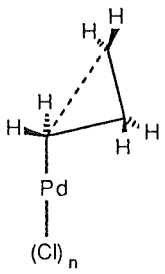
rising to 3.4:1 in chloroform with 1 % added ethanol. The authors proposed the product selectivity in the more polar solvents employed was due to a change to an SN_1-type mechanism with development of the tertiary cation resulting from corner attack, a consequence of the greater carbocation stability under the more polar conditions. Such a situation parallels the previously mentioned selectivity of nucleophilic attack in the oxymercuration of 1-phenylbicyclo[4.1.0]heptane.[40]

In a theoretical study of palladium(II) attack upon cyclopropane[56], it was found that different palladium(II) compounds behaved quite differently (Table 9), the ligands having a noticeable effect upon the calculated stabilities of the two intermediates (32) and (33). In commenting on the

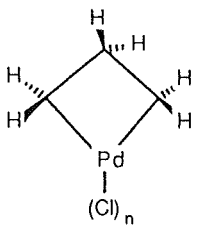
		Palladium Complex			
		Pd^0	$PdCl_2$	$PdCl_4^{2-}$	$PdCl^+$
corner attack	(32)	24	29.0		4.6
edge attack (Metallocyclobutane)	(33)	6	37.5	41.0	25.2
Edge transition State		17	19.8		

Table 9

Calculated interaction energies for various palladium complexes and cyclopropane (kcal mol^{-1}).



(32)

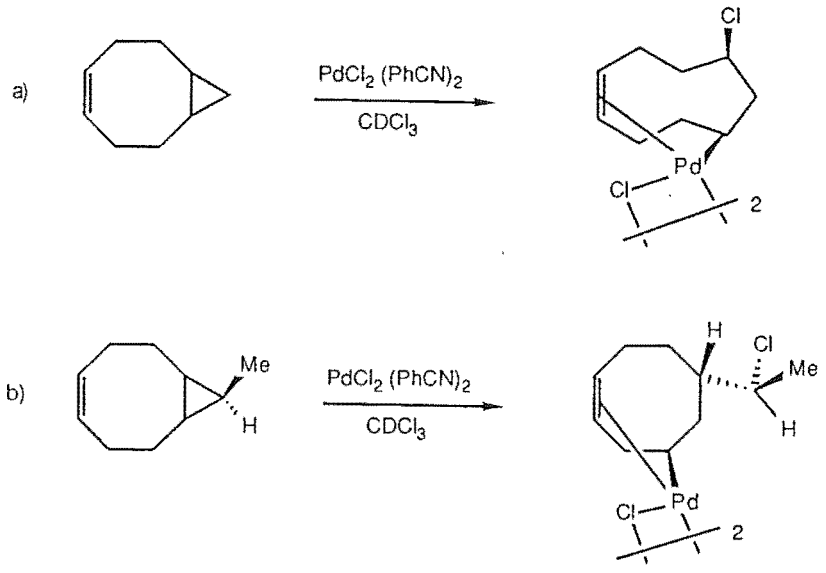


(33)

The overall charge is not shown for these structures as it is dependant upon the ligands.

chloropalladation of (+)-2-carene, the authors of the theoretical study note that raising the solvent polarity, which should favour formation of $PdCl^+$, results in an increase in product resulting from corner activation. However, no change in the rate of reaction of $PdCl_2$ to (+)-2-carene was observed upon addition of lithium chloride or cupric chloride[55], thereby showing the attacking species is not $PdCl^+$.

Charge stabilisation has been found to be important in the palladium(II) cleavage of substituted cyclopropanes, as examination of the reactions of cis-bicyclo[6.1.0]non-4-ene[57] and 9-exo-methyl-cis-bicyclo[6.1.0]non-4-ene[58] reveals. In the former reaction, palladium(II) cleaves the internal cyclopropyl bond to give a cis-chloropalladated product (Scheme 17a). Addition of a 9-exo-methyl to the reactant



Scheme 17

$PdCl_2(PhCN)_2$ addition to
a) Bicyclo[6.1.0]non-4-ene
b) 9-exo-methylbicyclo[6.1.0]non-4-ene.

results in external cyclopropyl bond cleavage by palladium(II) being favoured, the methyl group being better able to stabilise a developing positive charge. The product of this reaction

involves inversion at the centres attacked by both Pd(II) and Cl^- (Scheme 17b).[58]

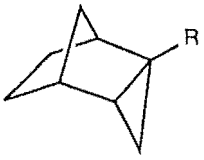
It Is therefore apparent that whether edge or corner attack by Pd(II) is observed will be dependent upon which electrophilic species exists in solution. This is at variance with the generally accepted view that transition metal induced cyclopropane ring openings proceed by oxidative addition. Indeed in the reactions of palladium(II) with cyclopropanes, it may be the corner pathway which is the more usual mechanism, the edge pathway requiring special circumstances to become favourable.

D Objects of this study

In spite of such quantitative studies, there has been, to date, no satisfactory explanation for the varied behaviour of cyclopropanes with differing electrophiles and metal ions. If such an explanation is found, the directed reaction of electrophiles with cyclopropanes will be of greater synthetic utility, leading to open chain compounds with as many as three asymmetric centres in a controlled relationship to one another.

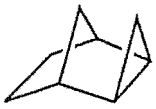
In an attempt to further define the factors which influence the reaction course of electrophiles with cyclopropanes, the reactions of selected tricyclo[3.2.1.$0^{2,4}$]octanes (-enes) (34) - (39) with various electrophiles- Hg^{2+} ($Hg(OAc)_2$ / MeOH); H^+/ D^+ (MeOH (D)/ TsOH); and Br^+ (Br_2 in either CCl_4 or MeOH) have been examined. These compounds encompass a variety of environments for the cyclopropyl ring and allow definitive conclusions to be made regarding the interaction of a substituted three membered ring

with electrophiles. The intermediate cations, once formed, may undergo rearrangement in addition to nucleophilic capture, such processes providing additional information on orbital overlap and charge development in these systems.

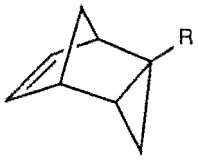


(34) R = H

(35) R = Me

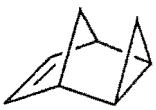


(36)



(37) R = H

(38) R = Me

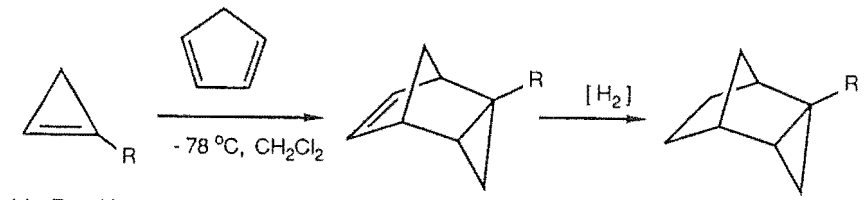


(39)

Chapter 2

A Preparation of compounds

The compounds chosen for this study were prepared by known procedures. endo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[59] (37) and 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[60] (38) were prepared by the addition of cyclopropene or 1-methylcyclopropene to a dichloromethane solution of cyclopentadiene at -78°C, and subsequently purified by spinning band distillation (Scheme 18). Hydrogenation of either (37) or (38) gave the saturated analogues endo-tricyclo[3.2.1.$0^{2,4}$]-octane (34) and 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) respectively.



(a) R = H
(b) R = Me

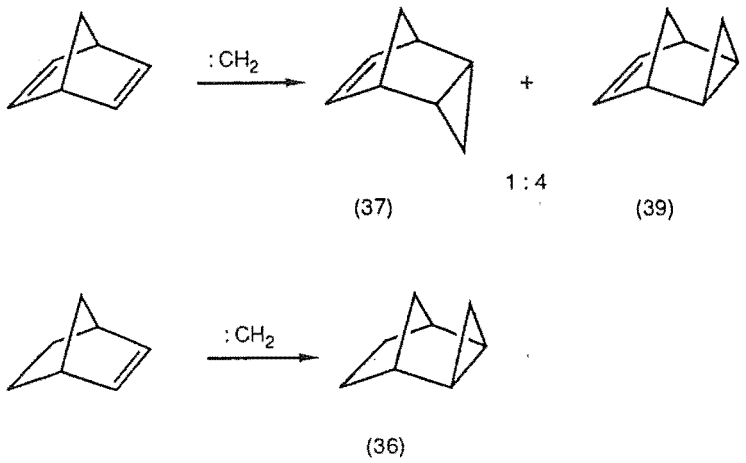
(37) R = H
(38) R = Me

(34) R = H
(35) R = Me

Scheme 18

exo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) and exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) were prepared by the addition of methylene carbene, generated from a zinc/copper couple[61] to norbornadiene and norbornene respectively (Scheme 19). While the reaction of norbornene with methylene carbene yielded only the exo- isomer (36), the corresponding reaction with norbornadiene yielded both exo- and endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) and (37) in the ratio of 4:1 respectively, consistent with reduced steric hindrance to

endo attack in the absence of the C5,C6 endo hydrogens.[62] Purification of exo- (39) was accomplished by precipitating the silver complex of (39), removing endo- (37) under vacuum and decomposing the complex of (39) by steam distillation.[63]



Scheme 19

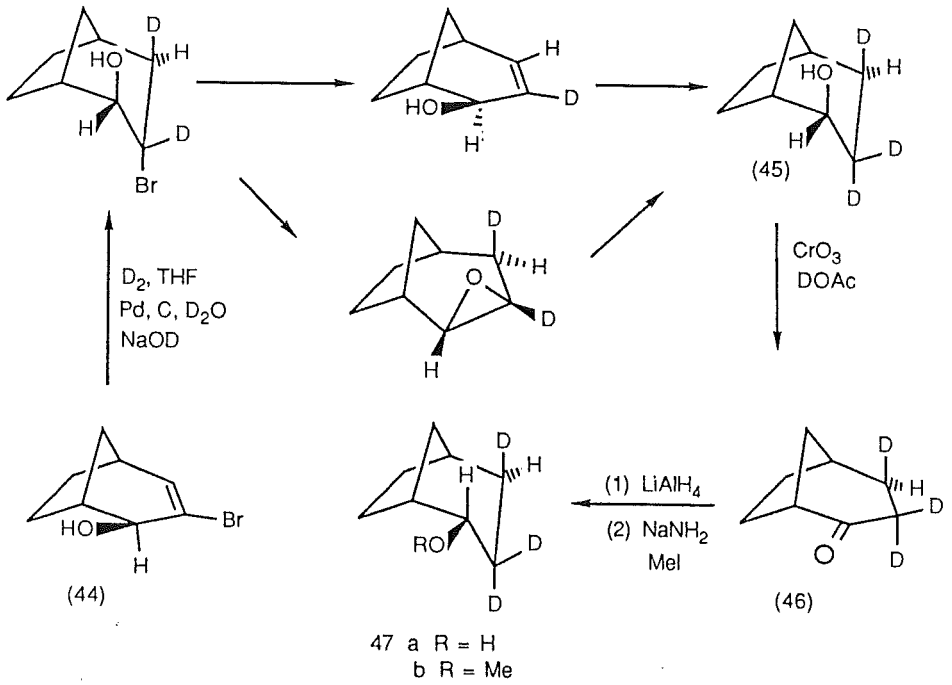
In the subsequent reactions of these compounds with proton (deuteron) or mercuric acetate, methanol was chosen as the reaction solvent, and hence nucleophile, in preference to acetic acid since an intermediate carbocation, when trapped by methanol, gives a product that is expected to be stable under the reaction conditions. In contrast, acetate products are often unstable and undergo further reaction, thus complicating analysis of the primary reaction pathway.[3]

B) Protonation and mercuration of endo-tricyclo[3.2.1.$0^{2,4}$]octane

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) with methanol and a catalytic quantity of p-toluenesulphonic acid gives a high yield of 2-endo-methoxybicyclo[3.2.1]octane (40a) when the reaction is carried out at 80°C for one week. A glc analysis of the reaction mixture indicated that the reaction had occurred to the extent of 80 % with less than 2 % of other products being formed. The axial nature of C2H in (40a), and hence the configuration of the methoxy group, was established by couplings of 10.1 Hz to H3-endo, 5.7 Hz to H3-exo and 3.0 Hz to H1, H1 being further coupled to H8a (6 Hz) and to H7-exo (6Hz). The ^{13}C nmr spectrum was assigned by comparison with the reported spectrum of 2-endo-hydroxybicyclo[3.2.1]-octane[64], a heteronuclear correlation experiment subsequently establishing the following connectivities: H1, 2.36 ppm / C1, 38.6 ppm; H2, 3.18 ppm / C2, 81.9 ppm; H3-exo 1.82 ppm and H3-endo 1.23ppm / C3, 25.7 ppm; H4-exo 1.33 ppm and H4-endo 1.41 ppm / C4, 31.0 ppm; H5, 2.12 ppm / C5, 34.4 ppm; H6-exo 1.65 ppm and H6-endo 1.34 ppm / C6, 28.8 ppm; H7-exo 1.73 ppm and H7-endo 1.50 ppm / C7, 23.9 ppm; and H8a 1.59 ppm and H8s 1.28 ppm / C8, 37.5 ppm. A detailed assignment of the spectrum was necessary in order to subsequently determine the stereochemistry of proton attack. The assignment of the chemical shifts of the C4 protons was not possible from the chemical shift differences or from difference NOE studies and was determined in the following manner. Bicyclo[3.2.1]heptan-2-exo-ol was prepared by the method reported by LaLonde[26] and a heteronuclear correlation experiment identified the connectivity of the C4-protons

centred at 1.65 ppm and 1.26 ppm with that carbon (28.3 ppm). The reported assignments of the ^{13}C nmr spectrum[64] of this alcohol are incorrect and C4, C6 and C7 are reassigned from coupling data obtained from the deuterated analogue (45). A difference NOE experiment showed that irradiation of the signal centred at 1.92 ppm and identified as H8s due to coupling with H8a, resulted in enhancement of the signal at 1.65 ppm which was therefore assigned to the C4-exo-H.

A deuterated analogue of 2-exo-hydroxybicyclo[3.2.1]-heptane (45) was prepared (Scheme 20) by reaction of 3-bromo-2-exo-hydroxybicyclo[3.2.1]hept-3-ene (44) with deuterium gas and sodium deuteroxide (1M) in deuterium oxide / tetrahydrofuran in the presence of palladium (10%) on carbon as catalyst. A signal at 1.26 ppm in the ^{1}H nmr spectrum and



Scheme 20

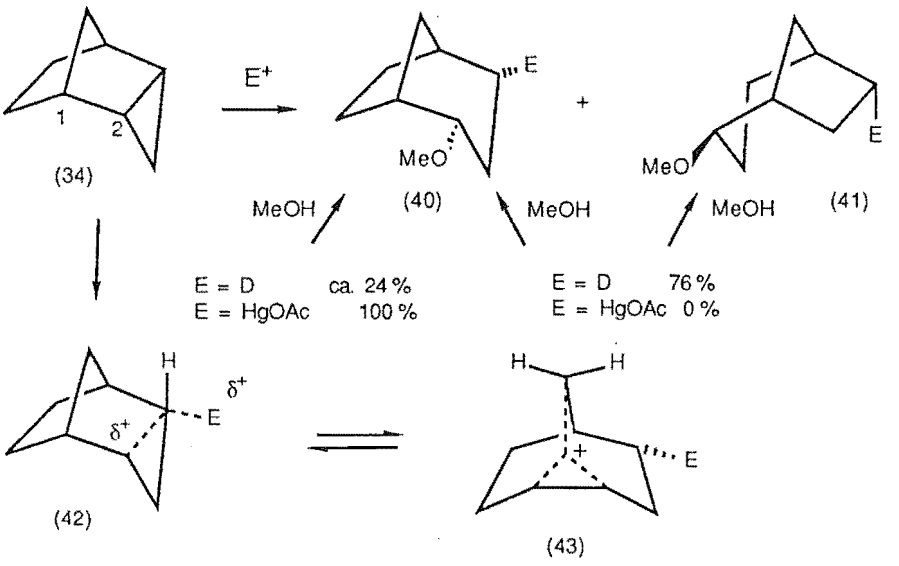
a triplet at 27.7 ppm due to C4 in the ^{13}C nmr spectrum demonstrate not only that this substrate contains deuterium at C4 but that the configuration of the proton at that carbon is endo. The ^{13}C nmr spectrum showed C3 as a multiplet consistent

with the presence of two deuterium atoms at this position. The mechanism for formation of this product may involve either reduction of an intermediate epoxide or loss of HBr (DBr) and deuterogenation of the resulting alkene. Oxidation of the alcohol with chromium trioxide-deuteroacetic acid gave the ketone (46), shown by analysis of the mass spectrum to contain on average 2.81 deuterium atoms. Lithium aluminium hydride reduction of this ketone where the deuterium configuration at C4 is known gave the endo-alcohol (47a) in a mixture (4:1) with the exo-alcohol (45) which was converted to a similar mixture of the 2-endo- and exo- methoxy compounds by reaction with sodium amide - methyl iodide. The chemical shifts of the C4 protons of the undeuterated substrate (40a) are centred at 1.33 ppm and 1.41 ppm. For the deuterated substrate (47b), with a known exo-configuration of deuterium at C4, the presence of a triplet in the carbon dimension exhibiting connectivity with a proton at 1.41 ppm in the proton dimension of a heteronuclear correlation experiment, allows the identification of this proton as endo. By exclusion the C4-exo-H of (40a) is centred at 1.33 ppm. The multiplicity in the heteronuclear correlation experiment of the signal at 1.41 ppm as a triplet results from C4-exo-deuterium coupling. This unambiguously establishes the assignment of the proton spectrum of the C4 protons in the parent compound (40a). A related procedure for determining deuterium stereochemistry which uses a heteronuclear correlation experiment has recently been reported.[65]

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) with mercuric acetate in anhydrous methanol at room temperature gave as a single product 4-endo-acetoxymercurio-2-endo-methoxy-bicyclo[3.2.1]octane (40c). The identity of this product was established in the following way. Reduction of (40c) with

sodium mercury amalgam in sodium hydroxide gave 2-endo-methoxybicyclo[3.2.1]octane (40a) identical with an authentic sample. The stereochemistry and position of the mercury in (40c) is consistent with the observed ^{1}H nmr couplings (selective decoupling), and ^{13}C-^{199}Hg couplings[66] (J ^{13}C-^{199}Hg: C1, 25 Hz; C2, 310 Hz; C3, 97 Hz; C4, 1634 Hz; C5, 66 Hz; C6, 65 Hz; C7, not obs.; C8, 310 Hz), but is in direct contrast with that previously predicted.[67]

In order to establish the reaction trajectory of the proton in the reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) with acidic methanol the reaction was carried out in methanol-d_1. The ^{13}C nmr spectrum of the product showed deuterium incorporation at both C4 and C6 (Scheme 21).



Scheme 21

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane with a) H^+ (D^+) b) $Hg(OAc)_2$

From the areas of the signals in the ^{2}H nmr spectrum at 1.41 ppm and 1.34 ppm the ratio of deuterium at these sites (40b:41b) was established as 62:38 respectively. The stereochemistry of the deuterium at C6 in (41b) was established as endo from its chemical shift. In the heteronuclear

correlation spectrum of the deuterated product mixture (40b,41b) the connectivities of the protons at C6 with that carbon were observed at 1.65 ppm and 1.34 ppm in (40b) and the protons at C4 with that carbon in (41b) at 1.33 ppm and 1.41 ppm. The presence of (41b) in the mixture was demonstrated from the heteronuclear correlation spectrum, which showed a triplet in the carbon dimension exhibiting connectivity with a proton at 1.65 ppm in the proton dimension for C6-exo-H, the additional splitting as a 1:1:1 triplet resulting from couplin of C6 to the endo-deuterium (Fig. 7). The endo-configuration

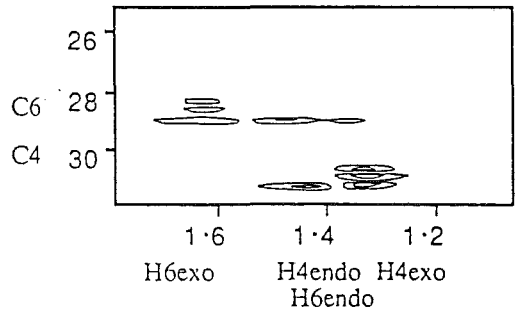


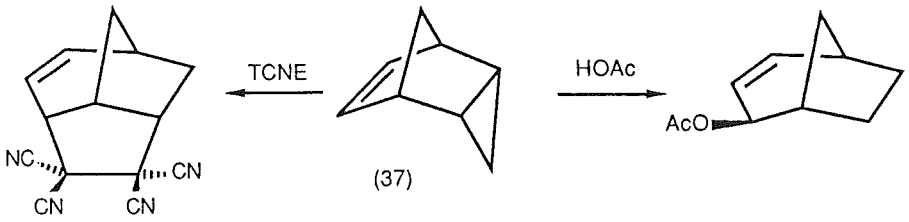
Figure 7

Heteronuclear correlation spectrum of a mixture (62 : 38) of 4-endo- and 6-endo-deutero-2-endo-methoxybicyclo[3.2.1]octane.

of the C6-D eliminated for this compound a signal at 1.34 ppm in the proton dimension and the presence of deuterium at C6 results in the signal at 1.65 ppm for the exo-H appearing as a triplet due to carbon deuterium coupling. The presence of (40b) in the mixture was similiarly identified by a triplet in the carbon dimension exhibiting connectivity with a proton at 1.33 ppm. The absence of the endo proton in (40b) eliminates a signal at 1.41 ppm and the signal at 1.33 ppm results from carbon-deuterium coupling and connectivity of C4 with the exo proton.

The formation of the two deuterated products (40b) and (41b) from reaction of (34) with deuteron in methanol can be accounted for if reaction of deuteron occurs exclusively at the corner of the cyclopropane with rupture of the more substituted adjacent cyclopropane bond. A protonated intermediate (42b) can be attacked by methanol to give (40b) or collapse to the protonated species (43b) which will be attacked with inversion equally at both C1 and C2. A small isotope effect will perturb the symmetry of the cation (43b) but the perturbation is expected to be sufficiently small not to affect the partition of the cation to (40b) and (41b) to any significant extent. The formation of rearranged product (41b) contrasts with the reaction with mercuric acetate in methanol where rearrangement is not observed. This is taken to indicate a greater degree of charge development at C4 in the reaction with proton. The preferential attack on hydrocarbon (34) by the nucleophile at C2 compared with C1 (62:38) demonstrates the protonated intermediate (42b) formed by corner attack of deuterium with inversion is trapped by nucleophile at least to the extent of 24 % before conversion to the symmetrical species (43b). This reflects competitive capture of the protonated cyclopropane before the activated complex has relaxed to any extent and before the structure has relaxed to the non-classical corner protonated cation (43). While nucleophilic attack on (42a) occurs with inversion to give (40a) further intramolecular reorganisation of the cation occurs to give (43a) where the configuration at C2 is retained. In this reaction it is apparent that intramolecular reaction with retention at C2 and intermolecular nucleophilic attack at C1 competes successfully with attack by methanol at C2.

The regioselective cleavage of the C2-C4 bond of hydrocarbon (34) with acid and with mercuric ions in the formation of (40) and (41) (Scheme 21) reflects either (i) the energy difference between the initially formed cations is such that there is a preference for protonation (mercuration) at C2 (or C4) as compared with C3, or (ii) subsequent rearrangement or nucleophilic attack at the C2-protonated (mercurated) hydrocabon (42) is more facile than reaction at the C3 protonated (mercurated) hydrocarbon. The reaction of (34) parallels that of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) with acetic acid[68] and with tetracyanoethene[69] (Scheme 22) and in both reactions it is the more substituted bond that is cleaved. A notable feature of the reactions of hydrocarbon (34) is that the attack by an external nucleophile is always observed to occur with inversion of configuration.



Scheme 22

Polarisation of the cyclopropane ring by an attacking electrophile (proton) has been found to be influenced by the low lying sigma orbitals present in the molecule.[29] For endo hydrocarbon (34), mixing of the low lying C1,C8/C5,C8 orbitals with the Walsh 3e'(S) and 3e'(A) cyclopropyl orbitals gives rise to the e_s and e_a molecular orbitals shown (Fig. 8). From photoelectron spectroscopy, the e_s orbital can be assigned as the HOMO at -9.40 eV, the e_a orbital at -10.20 eV.[70] Attack at the e_s orbital of necessity results in C2,C4 bond cleavage, electrophilic attack occurring with either retention or

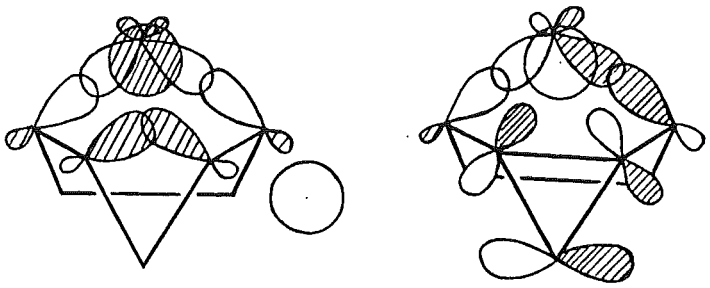


Figure 8

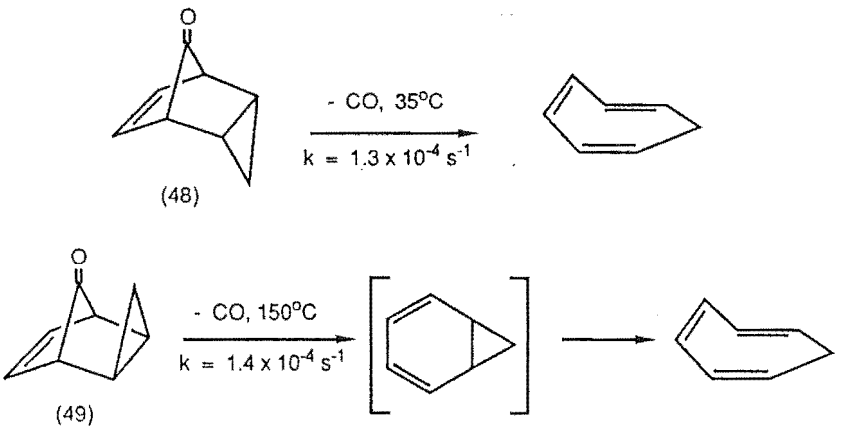
Overlap of the C1', C8 / C5, C8 σ orbitals with the cyclopropane orbitals.

inversion. For edge attack, while there is a favourable bonding interaction with the cyclopropyl 3e'(S) component of e_s, an unfavourable secondary orbital interaction with the C1,C8/C5,C8 orbitals disfavours such attack. For corner attack, a large antibonding interaction is not present, and hence this pathway is favoured. Interaction of orbitals of similar energy produces the greatest energy gain. Hence electrophilic attack at the energetically lower e_a molecular orbital and subsequent external cleavage is not as favourable as attack at the e_s HOMO, and this reaction pathway is not observed.

For deuteron attack at endo-tricyclo[3.2.1.$0^{2,4}$]octane, rearrangement accounts for a significant proportion (ca. 76 %) of the reaction pathway, consistent with the importance of cation stabilities. Such a consideration favours protonation at the corner of the C2 (C4) cyclopropyl ring, the developing positive charge at C2 being delocalised by interaction with the C1,C8 sigma bond. No such stabilisation is possible for the cations resulting from edge attack at C2 (C4) or attack at C3. Electrophilic attack by proton at the corner of the C2 (C4) cyclopropyl ring is exclusively observed, a consequence of both the favourable orbital overlap and carbocation stability.

Unlike proton attack, attack by mercuric acetate does not give rise to significant carbocation development in this reaction. Cation stability is therefore not as important and orbital overlap dictates the reaction pathway to give product resulting from C2,C4 cyclopropyl cleavage with inversion.

The influence of orbital overlap is similarly seen in the thermal decarbonylation of endo-tricyclo[3.2.1.$0^{2,4}$]octan-8-one (48)[71] (Scheme 23). The ease with which this compound



Scheme 23

Thermal decarbonylation of a) endo- b) exo-tricyclo[3.2.1.$0^{2,4}$]octan-8-one.

decarbonylates is rationalised by cyclpropyl participation, the C2,C4 cyclopropyl bond being favourably aligned for interaction with the C1,C8 and C5,C8 sigma bonds. In contrast, the corresponding exo- isomer (49) decarbonylates only at much higher temperatures (Scheme 23), and then by a different mechanism to the endo isomer.

Reduction of 4-endo-acetoxymercurio-2-endo-methoxy-bicyclo[3.2.1]octane (40c), the mercury adduct from reaction of (34) with mercuric acetate in methanol, with sodium mercury amalgam in sodium deuteroxide gave 4-endo-deutero-2-endo-methoxybicyclo[3.2.1]octane (40b). The ^{2}H nmr spectrum showed a signal at 1.43 ppm and a two-dimensional ^{1}H-^{13}C

heteronuclear correlation experiment identified the C4-exo-H at 1.35 ppm thereby establishing the configuration of the deuterium. The reduction conditions have been shown in related systems[66] to occur with retention of configuration and therefore the stereochemistry and position of the mercury in (40c) are unambiguous. Reduction with sodium borodeuteride was not stereospecific, and gave rise to 4-exo- and 4-endo-deutero-2-endo-methoxybicyclo[3.2.1]octane in the ratio of 45:55 respectively.

Formation of (40c) arises by attack of the mercuric ion at the corner of the cyclopropane ring with cleavage of the internal cyclopropyl bond and subsequent attack by methanol with inversion. The unsymmetrical mercurated cation (42c) does not rearrange to the more symmetrical corner mercurated cation (43c). It is suggested that a high degree of orbital interaction between C4 and C2 in the cation (42c) results in little charge development at C2 and therefore an absence of rearrangement. The reaction of mercuric acetate with a substituted cyclopropane is therefore similar to that of alkenes with mercuric acetate[72] where skeletal rearrangement is not normally observed.

The favoured attack by the electrophiles deuteron and mercuric ion and bromine[11] at the corner of the cyclopropane ring reflects the favourable interaction of both the degenerate HOMO's of the cyclopropane with the LUMO's of the proton (1s) or of the mercuric ion (6s) or bromine (4p) respectively (Fig. 9). It should be noted that for edge attack, while the HOMO/LUMO interaction is favourable for proton interaction with the symmetric Walsh orbital, this is not the case with the unsymmetric orbital. The preference for corner attack therefore reflects the favourable HOMO/LUMO interaction for

both degenerate molecular orbitals. However, for molecules where the 3e'(S) and 3e'(A) Walsh orbitals are no longer degenerate, reaction should be influenced by the HOMO, since this interaction will give the greatest energy gain upon interaction with the LUMO of the electrophile. Reaction at the next lower occupied molecular orbital becomes increasingly more probable as the energy difference between this orbital and the HOMO decreases, assuming the absence of any antibonding interactions for reaction at either molecular orbital. Hence, electrophilic attack at tetracyclo[3.3.0.$0^{2,4}$.$0^{3,6}$]octane, where the energy differential between the e_a HOMO and the e_s orbital is 0.85 eV[70b], would be expected to be different from reaction of the analogous exo-tricyclo[3.2.1.$0^{2,4}$]octane (36; Chapter3) with an energy difference between the e_s HOMO and the e_a orbital of 0.60 eV.[70a]

A favourable interaction of the LUMO $1a_2'$ (A) orbital of cyclopropane with the d-orbitals of electron donor metals allows oxidative addition[13,73] at the edge of the cyclopropane (Fig. 10). This interaction compensates for the more favoured sigma-interaction at the corner of cyclopropane between the HOMO Walsh orbitals and the LUMO orbitals of the electrophile. For ions with a filled d orbital the corresponding LUMO orbital will be the (n+1)s orbital, such as for the mercuric ion. However, for ions with an nd^8 electronic configuration, either the nd or (n+1)p orbitals may be chosen as the LUMO, this being a consequence of the generally low promotion energy for transition between these orbitals.[15] Since the donor ability[74] of the d_π-orbitals for mercury is small, the d_π-HOMO, cyclopropane LUMO interaction is considered unimportant. The reaction stereochemistry therefore parallels the reaction with deuteron.

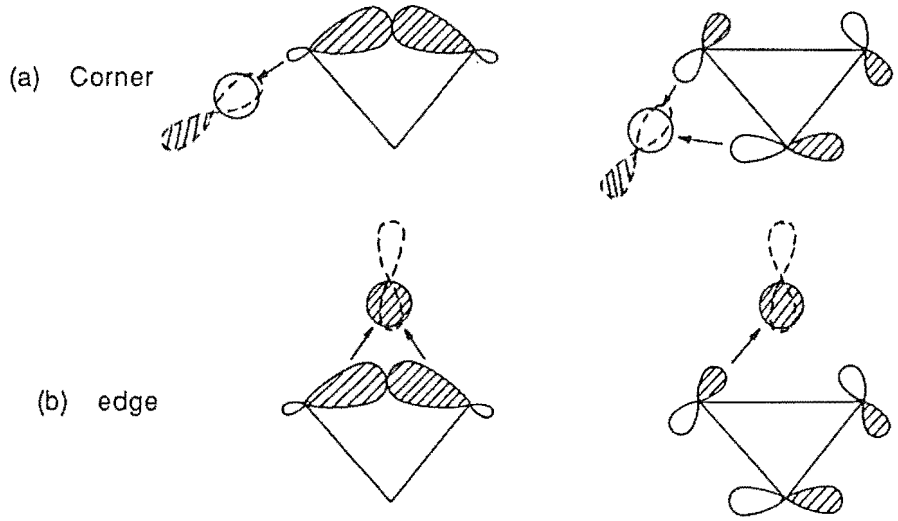


Figure 9

Sigma interaction of LUMO of electrophile with degenerate HOMO's of cyclopropane.

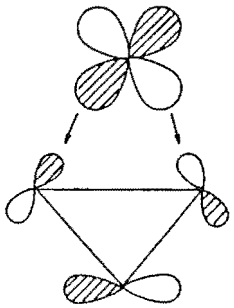


Figure 10

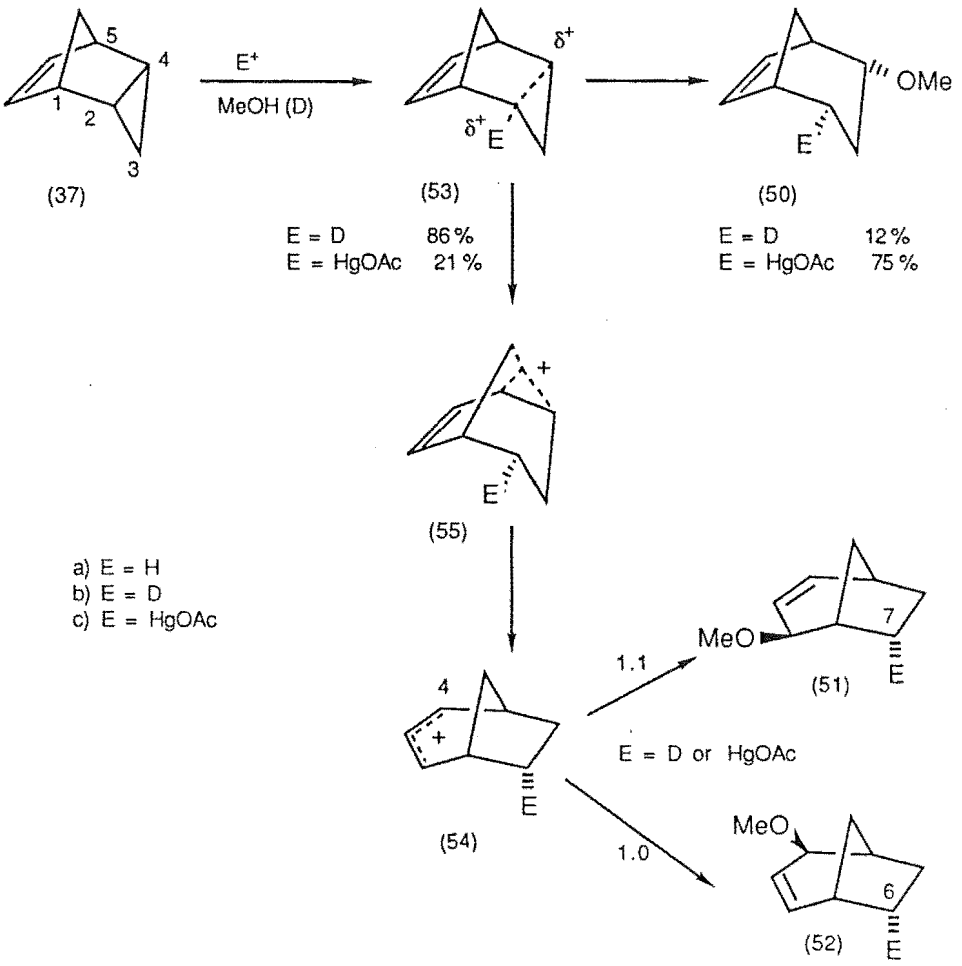
Back donation of d_{π} - electrons to LUMO's of cyclopropane.

Footnote: The stability of the methoxy ethers (40b) and (41b) was determined by heating the trideutero methoxy ether (47b) in p-toluenesulphonic acid, methanol for 7 days. The absence of rearranged product, as shown by ^{13}C nmr, indicates the 62:38 ratio of (40b):(41b) is kinetic in origin.

C) Protonation and mercuration of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene

The reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) with methanol-d_1, in the presence of a catalytic quantity of p-toluenesulphonic acid has been studied[75] to probe the stereochemistry of electrophilic attack. In undeuterated methanol the reaction gives three products: 2-exo-methoxybicyclo[3.2.1]oct-3-ene (51a), 2-endo-methoxybicyclo[3.2.1]oct-3-ene and 2-endo-methoxybicyclo[3.2.1]oct-6-ene (50a) in the ratio 86:2:12. When the reaction was carried out in methanol-d_1, the deuterium in the major product was incorporated at C6 and C7 in the ratio 1.0:1.1. The configuration of deuterium was endo defining the stereochemistry of proton (deuteron) attack on the hydrocarbon at C2 or C4 in the formation of the product. The preference for deuterium at C7 vs C6 shows that C4 of cation (54b), from which C8 has migrated, is marginally hindered relative to C2.

To probe the role of an electrophile in defining the reaction pathway, endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) was reacted with mercuric acetate in anhydrous methanol at room temperature (Scheme 24). While 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50c) was not separated from (51c) and (52c) it was present in sufficiently high yield in the reaction mixture to determine the ^1H and ^{13}C nmr parameters and unambiguously establish the structure. The C2-H (3.26 ppm) was axial, coupled with H1 at 2.77 ppm (3.2 Hz), H3-endo at 1.95 ppm (9.5 Hz) and H3-exo at 2.26 ppm (5.8 Hz); H4 centred at 2.73 ppm was axial, coupled to H5 at 2.88 ppm (2.5 Hz) and with H3-exo (5.6 Hz) and H3-endo (12.3 Hz).



Scheme 24

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with (a) H^+ (D^+) (b) $Hg(OAc)_2$

This establishes the mercurio and methoxy groups as adjacent to the C3-methylene and defines their stereochemistry. A homonuclear proton-proton correlation 2D nmr experiment further confirmed the structure of (50c) (Figure 11). The mercurio adducts were reduced with sodium mercury amalgam in sodium deuteroxide to give a mixture of 2-endo-methoxy-4-endo-deuterobicyclo[3.2.1]oct-6-ene (50b; 75 %), 2-exo-methoxy-6-endo-deuterobicyclo[3.2.1]oct-3-ene (52b; 10 %) and 2-exo-methoxy-7-endo-deuterobicyclo[3.2.1]oct-3-ene (51b; 11 %). The reaction conditions for reduction of the organo-mercurial mixture in related systems have been shown to give

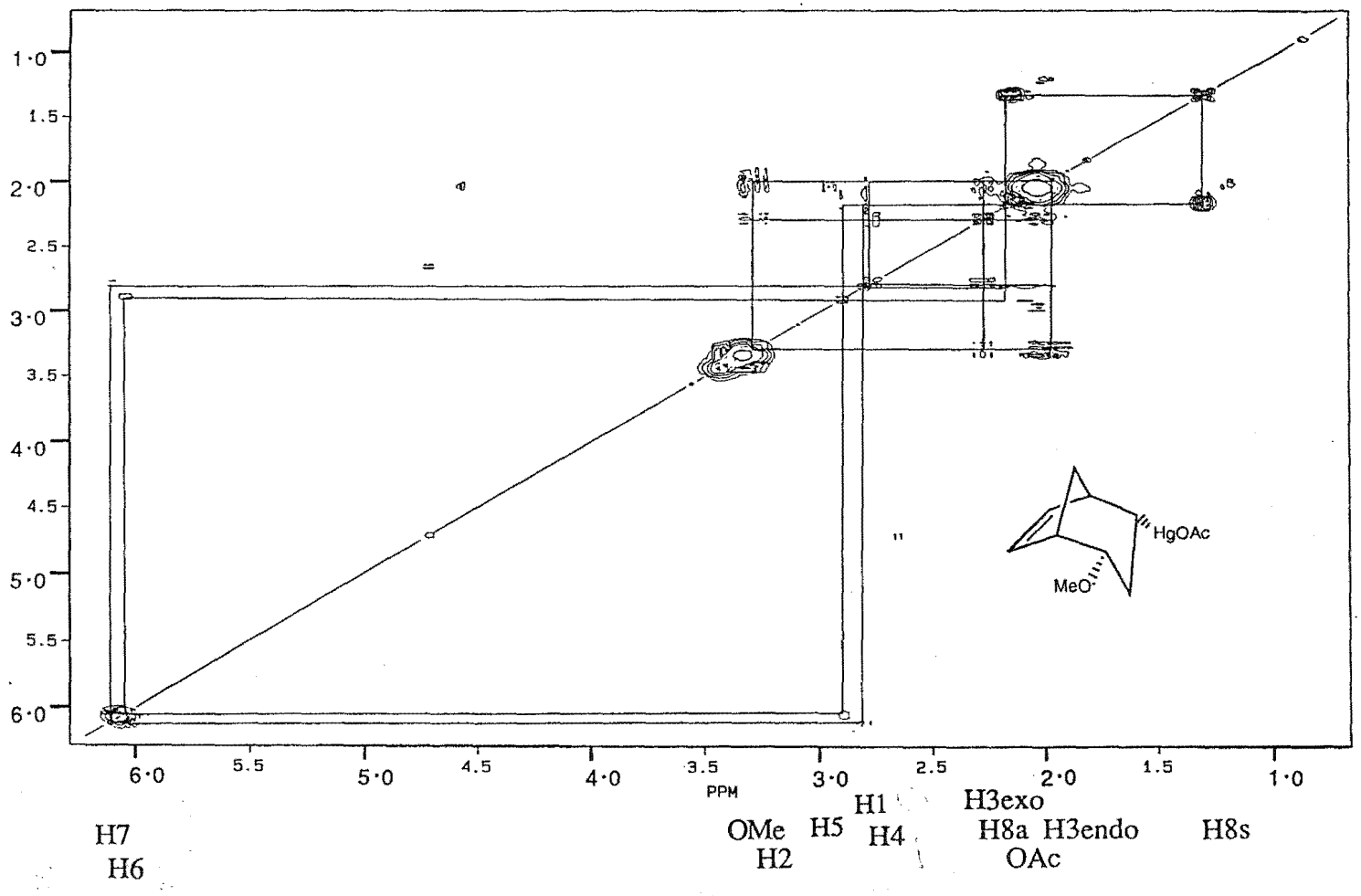


Figure 11

Homonuclear proton-proton correlation spectrum (COSY) of 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]oct-6-ene.

reduction with retention of configuration.[66] The identity of the minor products (51b / 52b), separated by preparative glc, follows from the known ^{1}H and ^{13}C nmr spectra[75] and in particular the configuration of the deuterium at C6 and C7 follows from the ^{2}H nmr spectrum which shows absorptions at 1.19 ppm (C6-endo-D) and 1.58 ppm (C7-endo-D) in the ratio 1.1:1.0. The ratio of these products [(51b) and (52b)] is notably the same as for the acid catalysed reaction of (37) with methanol-d_1 demonstrating that the cation (54c) exhibits some small memory effect with C4 marginally hindered relative to C2. The identity of (50a) isolated when the mercurio adducts are reduced in protic media follows from the ^{1}H nmr spectrum which showed H2 (3.19 ppm) coupled to H1 (J 2.7 Hz; 2.84 ppm) which is deshielded by the double bond, and to $(H3)_2$ (J 5.6, 9.3 Hz). The magnitude of the larger coupling to an adjacent H3 establishes the configuration of H2 as pseudo-axial. H1 and H5 are coupled to H8-anti (J 5.5 Hz) and the apparent absence of coupling to H8-syn is consistent with the geometry of the bicyclic [3.2.1] skeleton.[76] For the deuterated product (50b) obtained by reduction in deuterated media computer simulation using a Fortran LAME[77] program gave excellent agreement between the experimental and simulated spectra (Fig. 12). The magnitude of the coupling between H3-endo and an adjacent H4 (11.6 Hz) and the relatively small coupling of H3-exo and this proton (6.2 Hz) show the configuration of the C4-H (1.32 ppm) to be exo. The identity of this product confirms that reduction of (50b) under these conditions is stereospecific.

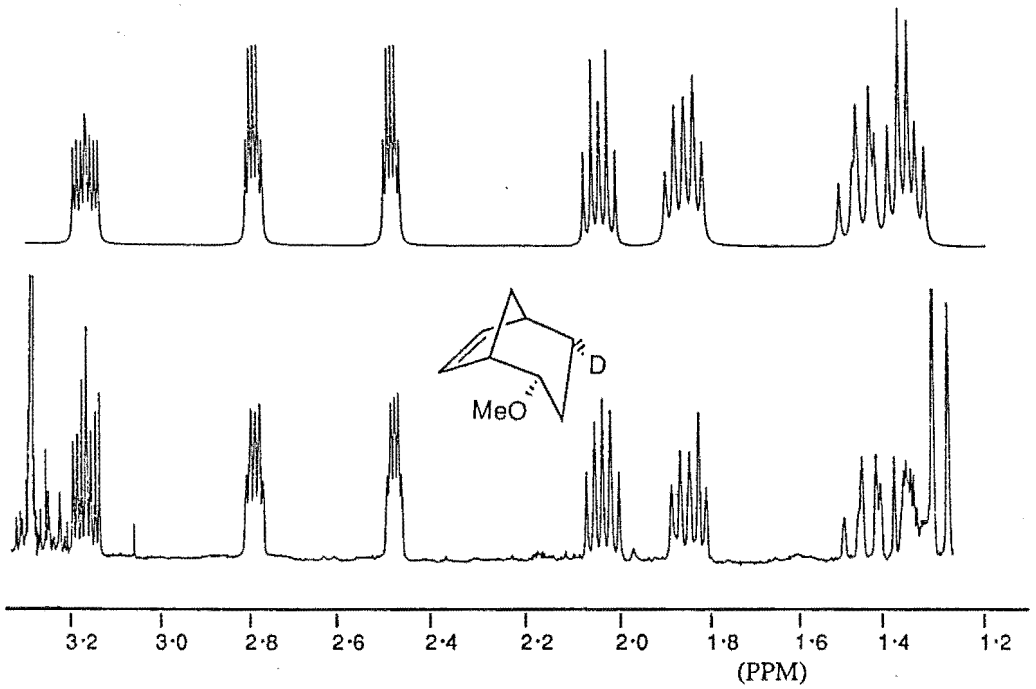


Figure 12

Top: Simulated spectrum of 4-endo-deutero-2-endo-methoxy-bicyclo[3.2.1]oct-6-ene.
Bottom: Actual spectrum (300 MHz).

The unsymmetrical mercurated cation (53c) in contrast to the deuterated analogue (53b) rearranges to only a limited extent via a symmetrical corner protonated cation (55) to the allylic cation (54c). A high degree of orbital interaction between C4 and C2 in the mercurated cation (53c) results in less charge development at C2 compared with the deuterated analogue (53b). The product (50c) is formed by capture of the mercurated species (53c) before it relaxes with substantial charge development at C4.

The minor product from reaction of hydrocarbon (37) with methanol-d_1 and p-toluenesulphonic acid was isolated by preparative glc and shown to be (50b). In the acid catalysed reaction this product, like the major product, is formed by stereospecific corner attack of the cyclopropane at C2 (C4). The ^2H nmr spectrum showed the C4-endo-D at 1.31 ppm and the protons H8a, H3-endo, H8s, H1 H2, H5, and H4-exo in the ^1H nmr

spectrum were identical* to those from the reduction of the organomercurial (50c).

The stereochemistry of deuterium in the product alkenes from reaction of hydrocarbon (37) with D^+ in methanol-d_1 and with mercuric acetate in methanol followed by stereospecific reductive deuteration precludes edge attack of the C2-C3 bond by D^+ and $Hg(OAc)_2$, and reorganisation to a corner species since such a process would require the attacking species to be exo in the products. The reactions proceed by electrophilic attack at the corner of the cyclopropane ring with inversion of configuration and proceed to a varying degree to undergo rearrangement to an allylic cation in a process which exhibits a small memory effect, and competes with capture of (53) to give (50). The corner atack of the electrophiles deuterium and mercuric ion parallels the reaction of tetracyanoethene with hydrocarbon (37) [69] (Scheme 22) and 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) [78] (Scheme 31).

Photoelectron spectroscopy shows that the two highest occupied molecular orbitals of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, assigned to the "π" and e_s orbitals respectively[70a] are relatively similar in energy. The HOMO will therefore contain a significant contribution from the cyclopropyl 3e'(S) orbital. Such a situation is found for tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene, where the second highest occupied molecular orbital (14a' or "π_2") was found to consist of 13 % π_1 character, corresponding to the C6,C7 double bond, 41 % π_2 character, from the C8,C9 double bond, and 29 % cyclopropyl 3e'(S) character[79],

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*Footnote: A minor contaminant exhibited a signal which overlapped with C3-exo-H but in all other respects the spectra were identical.

a result of mixing with the energetically similar e_s orbital. As a consequence of such mixing in endo hydrocarbon (37), overlap of the pi component of the HOMO with the electrophiles LUMO is not as favourable as with a simple alkene. From a consideration of orbital overlap, reaction by proton or mercuric acetate at the cyclopropyl ring is therefore competitive with double bond attack. In a manner similar to the reactions of the analogous endo-tricyclo[3.2.1.$0^{2,4}$]octane, electrophilic attack at the cyclopropyl ring occurs with inversion at C2 (C4). This reflects the destabilisation of edge attack at C2,C4 due to an unfavourable secondary orbital interaction between the electrophiles LUMO and the C1,C8,C5 component of the hydrocarbon HOMO. For proton attack stabilisation of the positive charge at C2 from interaction with the C1,C8 sigma bond and the inherent greater rate of reaction of a proton with a cyclopropane ring as compared with a double bond[23a] gives rise to the exclusive cyclopropyl ring cleavage observed.

This kinetic preference for cyclopropyl attack as compared to double bond attack by proton can be rationalised by examination of the heats of reaction of the initially formed cations. The profiles of minimum energy for the reaction of proton with alkene or cyclopropane allow assignment of heats of reaction ΔH_r (a) and ΔH_r (b) / ΔH_r (c) to the classical cation (56) [80] and the non-classical cations (57) / (58) respectively (Figure 13). Numerically, ΔH_r (a) will be larger than ΔH_r (b) or ΔH_r (c), this difference mainly reflecting the additional stability to be derived from delocalisation of the positive charge in cations (57) / (58). However, such a term will be energetically significant only if the cations (56) and (57) / (58) are similarly substituted. Support for such a

rationale can be found by a comparison of the relative heats of reaction, as obtained from the theoretically calculated cation stabilities (heats of formation) and the experimentally determined heats of formation of the alkene or cyclopropane. Dependent upon which basis set is employed it is found that formation of cation (56), from proton attack at ethylene, is energetically less favourable than formation of cations (57) or (58) by 4.2 to 11.0 kcal mol^{-1} (Appendix A).

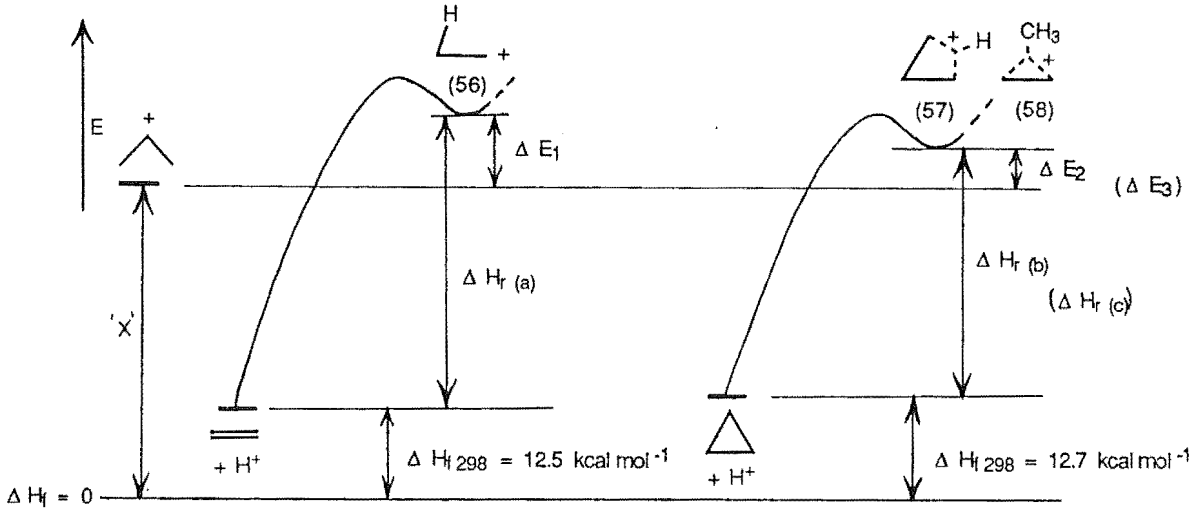

Figure 13

For mercuric acetate attack at a cyclopropyl ring or alkene, intermediate cations of the type (60) and (59)[80] will have heats of reaction ΔH_r (e) and ΔH_r (d) respectively (Figure 14). The heats of reaction for these intermediate cations will be energetically closer than (56) and (57) / (58) from attack by proton, a consequence of the presence of special stabilisation mechanisms for cations (59)* and (60). In comparison for the reaction with proton, such a stabilisation is operative only for cyclopropyl attack.

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*Footnote: Cation (59) has been shown to be stabilised by hyperconjugation.[39]

Unlike the reaction of proton with alkene or cyclopropane, the corresponding reactions with mercuric acetate are thought to be sterically sensitive (Chapter 1). The activation energy, and therefore the heat of formation[81] (and hence the heat of reaction) will all have a steric component.

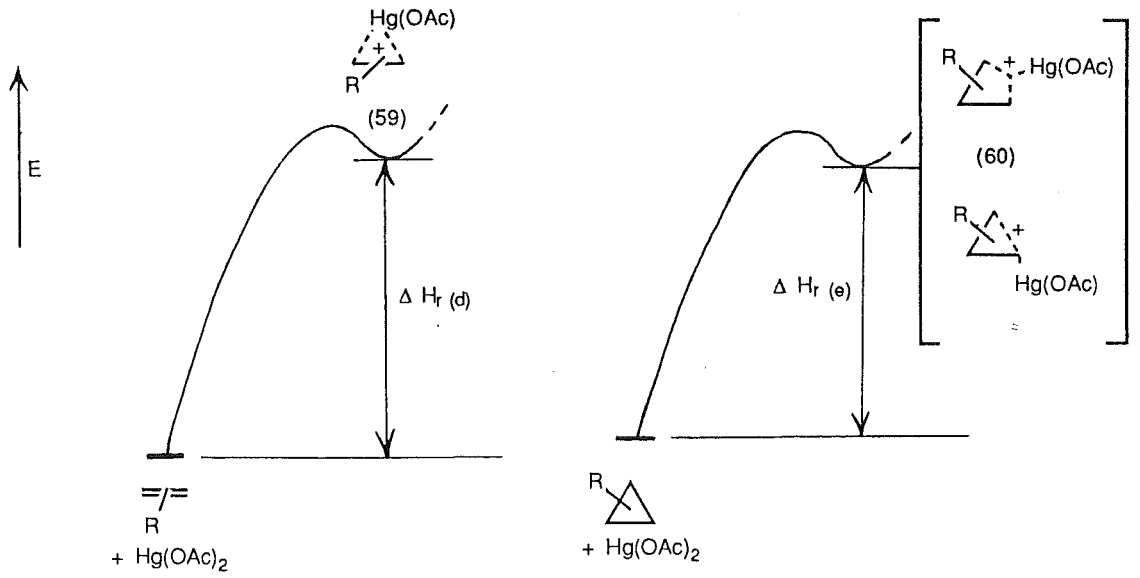


Figure 14

For electrophilic cleavage of a cyclopropyl ring and electrophilic attack at a double bond by proton[3,29,80], $Hg(OAc)_2$[80] or bromine[80] the attack by the electrophile is at least partially rate determining. It is therefore appropriate to compare the relative heats of reaction of the carbocations as a measure of the preference for attack at different sites in the reactant molecule.

Mercuric acetate will preferentially attack the cyclopropyl ring if the intermediate carbocation is stabilised relative to the carbocation produced by reaction with a double bond. However, attack at the double bond will be favoured if steric accesibility to the pi system is more favoured than that at the cyclopropyl ring, or if electronic factors (eg: electron withdrawing substituents) destabilise attack at the

cyclopropane ring. In the present reaction of mercuric acetate with endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, the absence of destabilising orbital factors for cyclopropyl cleavage and the presence of stabilisation for the cations (55c) and (54c) by delocalisation, coupled with the absence of overriding steric constraints favours attack at the cyclopropyl ring. Attack at the pi system does not appear to be particularly hindered but the absence of a similar stabilisation for the so produced mercurinium ion makes this process kinetically uncompetitive. The limited rearrangement observed in this reaction to the allylic cation (54c) indicates the inherent stability of the mercurated cyclopropane (53c) relative to other cations.

The lack of substantial charge development on carbon for cyclopropyl attack by mercuric acetate, and hence the lack of rearrangement often observed, can be considered a consequence of the relatively poor overlap between the mercury 6s orbital and the cyclopropyl 3e' orbitals. For attack of a proton at a cyclopropyl ring perturbation of the HOMO of cyclopropane at C1 to give a more favourable carbon-hydrogen overlap occurs with a substantial decrease in bonding between C1 and C2 and greater charge development at C2. For attack by mercury the overlap between the mercury and the cyclopropane HOMO is less efficient and as a consequence the bonding between C1, C2 is reduced to a lesser extent, thereby accounting for the lesser development of positive charge at C4 (Figure 15). However, if delocalisation of the positive charge from the mercury to carbon is energetically favourable (ie: there is a decrease in C1, C2 bonding in the cyclopropyl ring) then we would predict rearrangement would occur where possible. Such is the situation found in the mercuration of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, rearrangement accounting

for 21 % of the reaction pathway. The driving force for rearrangement is the inherent stability of the allylic cation (54c), electron donation from the C1,C8 sigma bond facilitating rearrangement to this species.

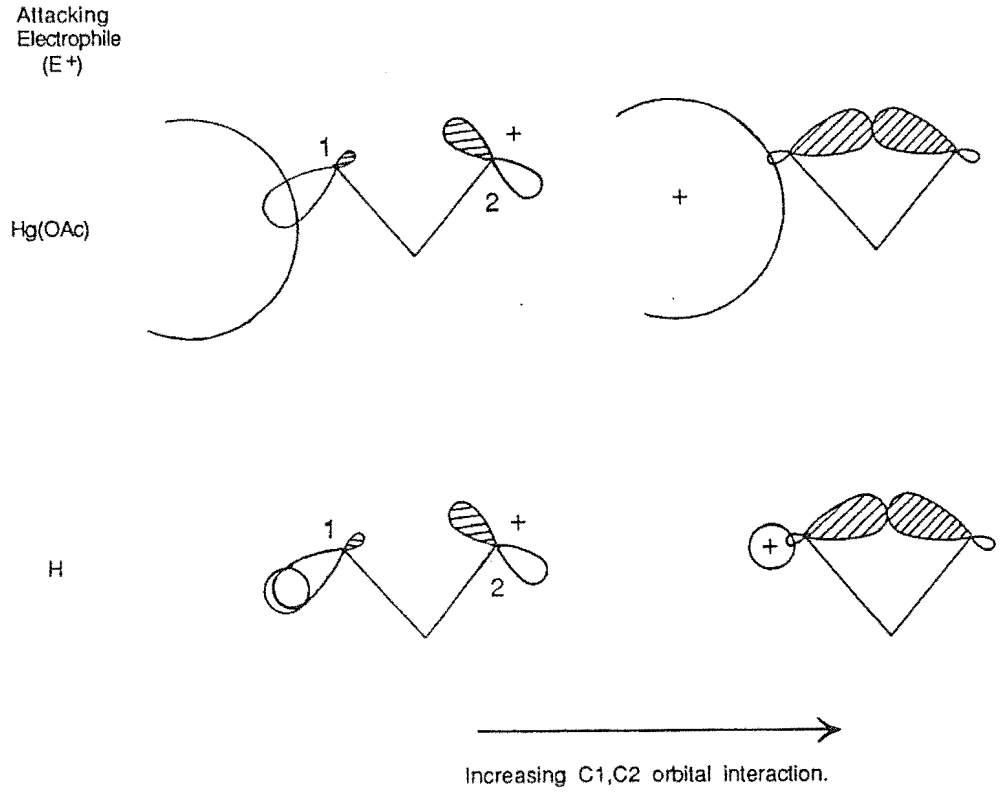


Figure 15

Appendix A

A heat of formation 'x' can be assigned to the 2-propyl cation (Figure 13). Hence,

$$\Delta H_{r\ (m)} = (x - \Delta H_{f\ 298} + \Delta E_n),$$

$\Delta H_{r\ (m)}$ being the heat of reaction for proton attack at alkene or a cyclopropane, $\Delta H_{f\ 298}$ the heat of formation of alkene or cyclopropane[82] and ΔE_n the energy of the cation relative to the 2-propyl species.

For proton attack at ethylene, employing the HF 6-31G** basis with HF/6-31G* geometries[16] shows

$$\Delta H_{r\ (a)} = (x - 12.5 + 21.6)\ \text{kcal mol}^{-1}$$

$$= (x + 9.1)\ \text{kcal mol}^{-1}$$

Using the same basis set[16], it can be shown that cations (57) and (58) have heats of reaction

$$\Delta H_{r\ (b)} = (x + 4.9)\ \text{kcal mol}^{-1} \text{ and}$$

$$\Delta H_{r\ (c)} = (x + 1.0)\ \text{kcal mol}^{-1} \text{ respectively.}$$

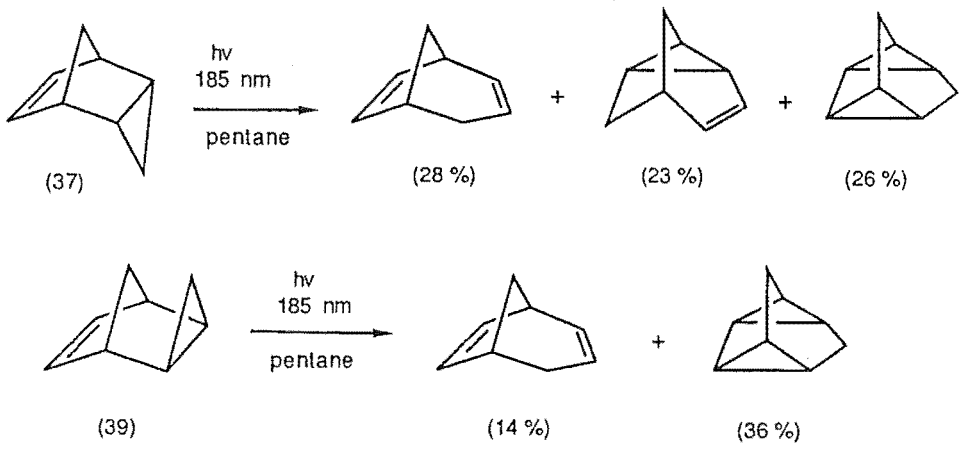
Thus, cation (56) is destabilised relative to cations (57) and (58) by 4.2 and 8.1 kcal mol^{-1} respectively.

Since $\Delta H_{f\ 298}$ applies to the compound in its standard state at STP (298 K, 1 atm.), the above approximation for the rate of protonation of ethylene or cyclopropane is valid only for a gas phase reaction. However, the same principles will be expected to hold for protonation of the higher (liquid) homologues.

Chapter 3

A) Introduction

To examine the effect orbital environment about a cyclopropane ring has on the reaction course, the electrophilic attack at exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) and exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) were examined and compared with those of the corresponding endo isomers (34) and (37). The chemical consequence of such differences in structure is known for the photochemistry of these compounds- photolysis of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) yielding three products (Scheme 25) while irradiation of the analogous exo isomer (39) yields one major and one minor product.[83] Such differences are thought to be a consequence of the differing interactions of the cyclopropyl ring with the pi system.



Scheme 25

Photochemical reactivity of endo- and exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene.

Since the developing carbocations in the reactions of exo (36) and (39) will be of a different structure than those formed in the reactions of the corresponding endo substrates (34) and (37), the ability of proximate sigma bonds to assist in the

polarisability of the cyclopropyl bond will be reflected in the reaction course.

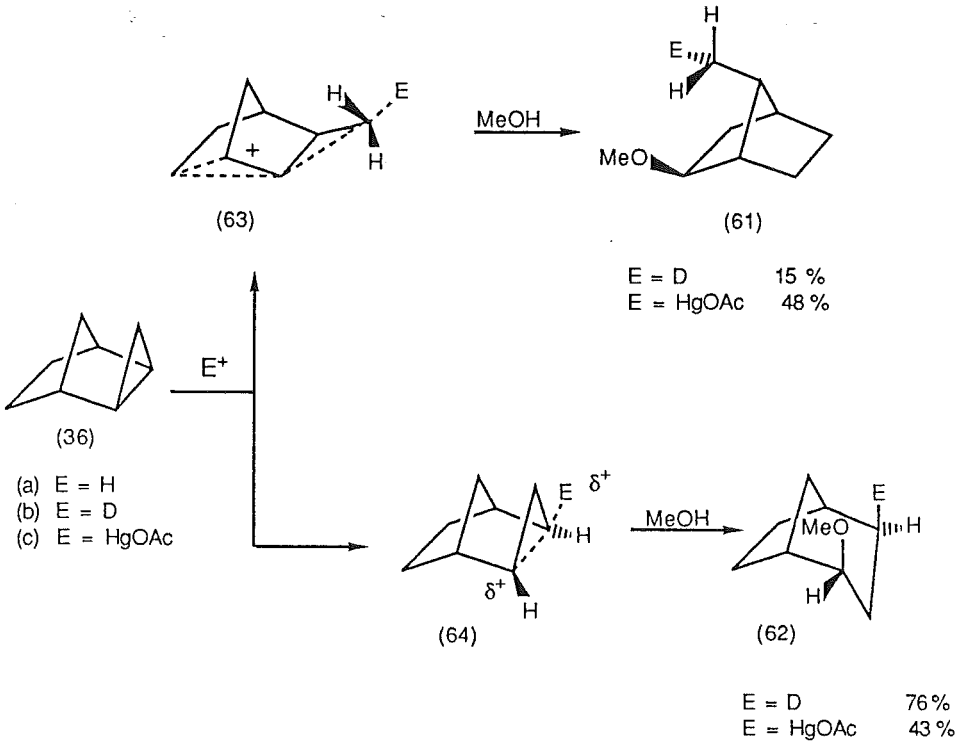
B) Protonation and mercuration of exo-tricyclo[3.2.1.$0^{2,4}$]octane

LaLonde some years ago[84] studied the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]octane with sulphuric acid in acetic acid and observed by glc five acetate products, only two of which were identified. After hydrolysis, bicyclo[3.2.1]octan-2-exo-ol and 2-hydroxybicyclo[2.2.2]octane were found to be present in 35 % and 22 % yield respectively. Both of these products result from cleavage of the internal cyclopropyl bond.

We have investigated the reaction of this hydrocarbon with acidic methanol and with mercuric acetate in methanol. The acid catalysed reaction in methanol would be expected to give a less complex reaction mixture than observed by LaLonde since the initial products of reaction under these conditions are expected to be stable. The reaction with methanol in the presence of p-toluenesulphonic acid was followed by glc and gave 2-exo-methoxybicyclo[3.2.1]octane (62a) and 2-exo-methoxy-7-syn-methylbicyclo[2.2.1]heptane (61a) in 76 % and 15 % yield respectively (Scheme 26). These products were separated by preparative glc. The identity of 2-exo-methoxybicyclo[3.2.1]octane (62a) follows from the ^{1}H and ^{13}C nmr spectra and by its identity to an authentic sample prepared by reaction of 2-exo-hydroxybicyclo[3.2.1]heptane, prepared as previously outlined (Chapter 2), with sodium amide - methyl iodide.[85]

The identity of 2-exo-methoxy-7-syn-methylbicyclo-

[2.2.1]heptane (61a) follows from a heteronuclear correlation spectrum in conjunction with coupling data (selective decoupling) and difference NOE's. The coupling of the C1-H (2.10 ppm) to the C6-exo-H (3.1 Hz), and C4-H (1.95 ppm) to C3-exo-H (3.0 Hz) and C5-exo-H (3.0 Hz), establishes that either the methyl or the methoxy group is at C2 and in an exo configuration. A difference NOE experiment

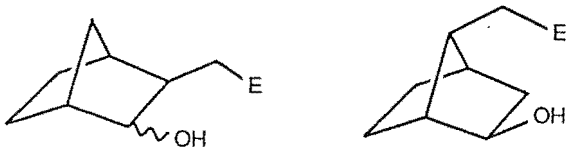


Scheme 26

Reaction of exo-tricyclo[3.2.1.$0^{2,4}$]octane with
a) H^+ (D^+) b) $Hg(OAc)_2$

showed that on irradiation of H4 (1.95 ppm) the signal of the methyl was enhanced as well as the $C3H_2$ (1.73 ppm), C5-exo-H (1.5 ppm) and C5-endo-H (1.05 ppm). Irradiation of H2 and the methoxy-protons, both centred at 3.27 ppm, caused enhancement of H1 (2.10 ppm), $C3H_2$ (1.73 ppm) and the methyl at 1.05 ppm thereby establishing that the methoxy group is at C2 and the methyl in a syn configuration at C7. The ^{13}C nmr was assigned by comparison with that of the known 7-syn-methylbicyclo[2.2.1]heptan-2-exo-ol.[86]

Reaction of the hydrocarbon (36) with mercuric acetate in water followed by reduction of the intermediate hydroxy acetoxymercurio adducts and subsequent oxidation has been reported[67] to give a 1:9 mixture of 3-exo-methylbicyclo-[2.2.1]heptan-2-one and 7-syn-methylbicyclo[2.2.1]heptan-2-one respectively. This implicates (65c) and (66c) as initial reaction products, the stereochemistry of the alcohol functionality in (65c) not having been established. Both products result from external bond rupture involving mercury attack at C3. When the reaction of (36) with mercuric



(65) (66)

a) E = H
b) E = D
c) E = Hg(OAc)

acetate was repeated, but in methanol as solvent, (61c) and (62c) were formed in about equal amounts. The mercuric compounds were not able to be separated and therefore were reduced with sodium mercury amalgam in sodium hydroxide to give the corresponding methoxy-hydrocarbons (61a) and (62a) in 48 % and 43 % yields respectively. These two products were separated by preparative glc and shown to be identical in all respects to the products obtained from reaction of the hydrocarbon with methanol in the presence of p-toluenesulphonic acid. The observation of mercuric ion cleavage of the most substituted cyclopropane bond in the formation of (62c) is in direct conflict with previously stated rules for mercuric ion induced cyclopropane ring opening[72] and at variance with the previously reported reaction of mercuric acetate in water.[67]

LaLonde[26] has reported the reaction of hydrocarbon (36) with sulphuric acid-d_2 in acetic acid-d_1 and analysed the stereochemistry of the incorporated deuterium in the major product by conversion of the product acetate into hydrocarbon and comparison of the infrared spectrum of the deuterated hydrocarbon with the infrared spectrum of authentic exo- and endo- C2-deuterated-bicyclo[3.2.1]octane. This study concluded that the deuterium was exo consistent with deuterium attack at the corner of the cyclopropyl unit.

It was decided to investigate the reaction of the exo-hydrocarbon (36) with methanol-d_1 and deuteron. The mass spectrum of the product deuteromethoxy hydrocarbon (62b) showed the deuterium content of the sample to be 90 % d^1. A heteronuclear correlation experiment on undeuterated sample established the C4-exo-H at 1.62 ppm and the C4-endo-H at 1.38 ppm. For the deuterated sample a ^2H nmr spectrum exhibited a signal for the C4-exo-D at 1.62 ppm and a heteronuclear correlation experiment exhibited a triplet in the carbon dimension exhibiting connectivity with C4-endo-H at 1.38 ppm in the proton dimension (Fig. 16). The splitting results from coupling of C4 to the exo-deuterium. Furthermore, a difference NOE showed that irradiation of H8s at 1.84 ppm caused no enhancement of the signal of the 4-endo-H at 1.38 ppm, further confirming the configuration of deuterium at C4. The presence of deuterium in the methyl of (61b) was established from the ^{13}C nmr spectrum which showed the methyl carbon as a 1:1:1 triplet at 12.7 ppm.

For reaction of the exo-hydrocarbon (36) with mercuric acetate in methanol the intermediate mixture of mercuric salts was reduced with sodium mercury amalgam in sodium deuteroxide. The product (61b) was identical with that obtained previously

from the acid catalysed reaction of (36) with methanol-d_1. The ^2H nmr spectrum of 2-exo-methoxy-4-exo-deuterobicyclo[3.2.1]-octane (62b) showed a signal at 1.62 ppm and the product was identical in all respects to that obtained from the reaction with acidic methanol-d_1 thereby establishing that the mercury

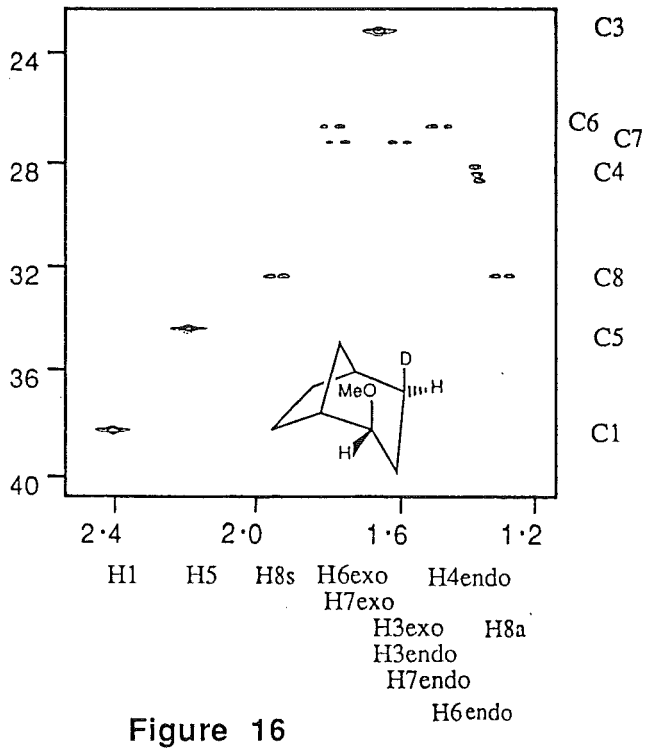


Figure 16

Heteronuclear correlation spectrum of 4-exo-deutero-2-exo-methoxybicyclo[3.2.1]octane.

attacked the cyclopropyl ring with inversion. Notably, for cation (63) a 6,2 hydride shift does not compete with capture of the intermediate cation by methanol, consistent with delocalisation from the C3 mercurated species to C1 as shown in Scheme 26.

For exo hydrocarbon (36), mixing of the Walsh 3e'(S) and 3e'(A) orbitals with the C1,C7/C5,C6 orbitals of the correct symmetry gives rise to the HOMO e_s and the e_a orbitals shown (Fig. 17). Since the separation between the e_s and e_a orbitals for exo (36) is not as large as for endo (34)[70a], the corresponding energy gains from a mixing of the HOMO/LUMO will not be as great. For attack at the e_s orbital, corner attack

results, which is considered a consequence of the destabilisation of edge attack due to an unfavourable secondary orbital interaction with the C1,C7/C5,C6 orbitals (Fig. 18). However, for external cleavage attack at the e_a orbital could result in either edge or corner attack. Experimental

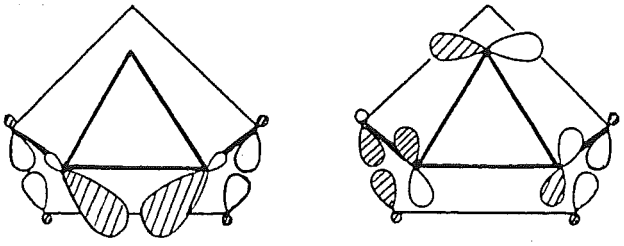


Figure 17

Mixing of the 3e'(S) and 3e'(A) orbitals with the C1, C7 / C5, C6 sigma orbitals to give the e_s HOMO and the e_a molecular orbital.

determination of the stereochemistry of electrophile attack was not possible due to the presence of the prochiral C8 methylene in product (61). For proton attack at hydrocarbon (36), the preference for attack at the e_s HOMO reflects the energy gains from the HOMO/LUMO interaction. However since the energy gap between e_s-e_a is not too large, and delocalisation stabilises cation (63a) produced from attack at the e_a orbital, this pathway is competitive. For attack by mercuric acetate on (36), any steric hinderance to corner attack at the e_s orbital is offset by the gains in the favourable e_s HOMO/mercury 6s LUMO interaction. Attack by mercuric acetate at the e_a orbital is however more competitive than for proton attack at (36).

The apparent contrast of complete external cyclopropane ring cleavage in the mercuration of <u>exo</u>-tricyclo[3.2.1.$0^{2,4}$]-octane (36) in water, and the similar ratio of external to internal cleavage of (36) observed for mercuration in methanol,

suggests the relative stabilities of the two cations (63c) and (64c) in the solvents methanol and water are different. While the carbocationic nature of (64c) is low, the positive charge residing largely at the mercury (Chapter 2), this is not the situation for (63c). Since (63c) will be more sensitive to solvent polarity than (64c), it will be destabilised more in

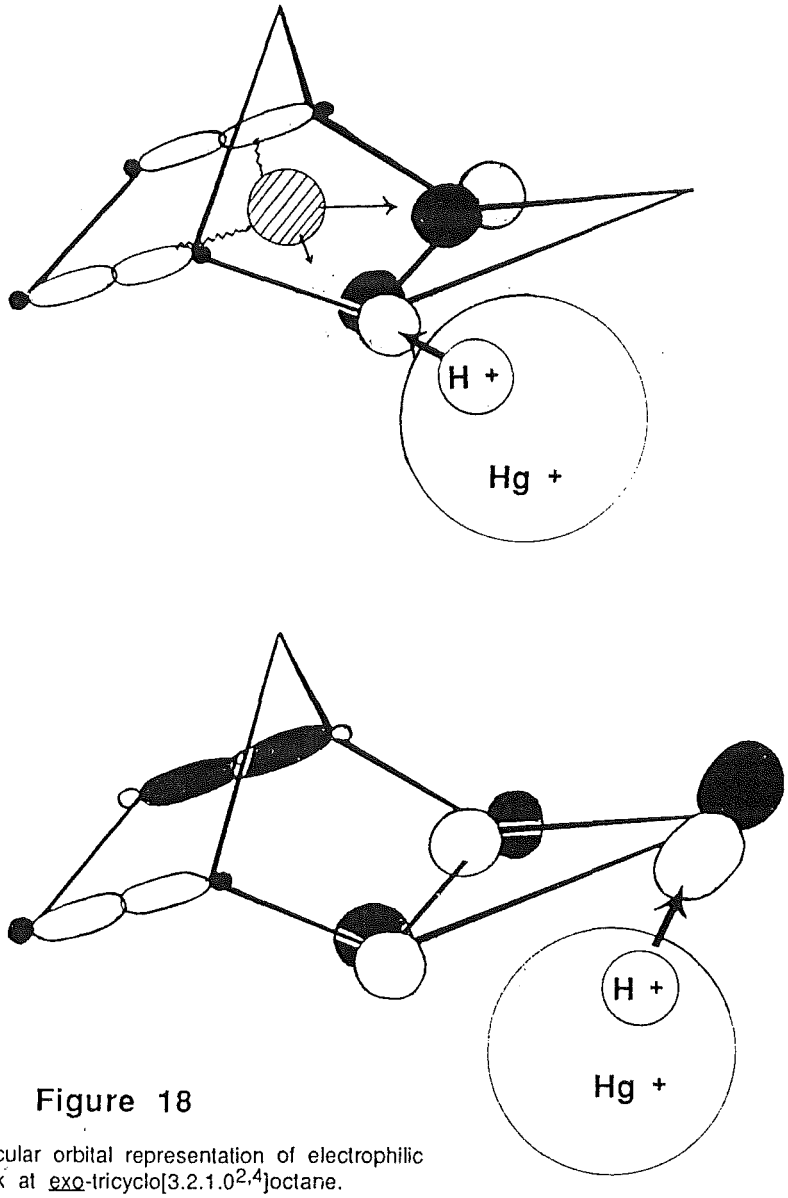


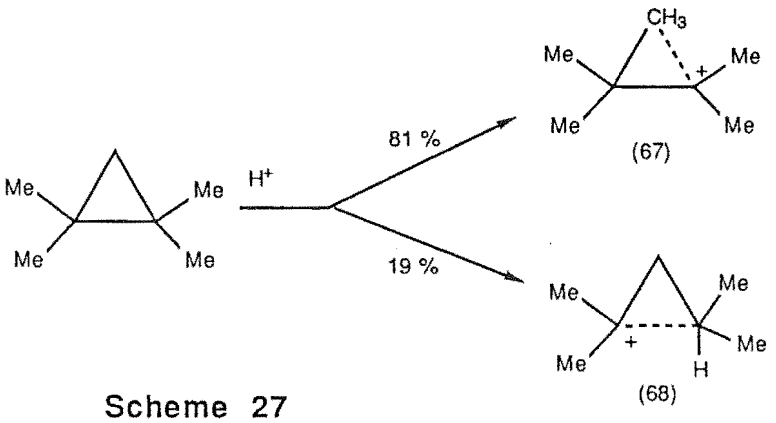
Figure 18

Molecular orbital representation of electrophilic attack at exo-tricyclo[3.2.1.$0^{2,4}$]octane.

methanol than in water than will (64c). In methanol, the destabilisation of (63c) is such that the sterically less favoured attack at the e_s HOMO is competitive. However, with water as a reaction solvent, cation stabilities are no longer

as important and mercuric acetate attacks at the site of greatest steric accessibility, namely the e_a orbital at C3.

The formation of (61c) and (62c) resulting from cleavage of different cyclopropyl bonds parallels the acetolysis of 1,1,2,2-tetramethylcyclopropane.[3] In this reaction (Scheme 27), products resulting from cleavage of the most substituted bond along with products from rupture of the adjacent bond are



Scheme 27

Bond cleavage in the acetolysis of tetramethylcyclopropane.

observed. Wiberg[3] has calculated that for the reaction of the tetramethylcyclopropane with a proton there is not a strong preference for which bond is cleaved. He argues that the comparability in calculated energy of cations (67) and (68), which are presumed to lie along the reaction coordinate, rationalises the observation that the electrophile does not have a strong preference for which bond is cleaved. Nevertheless these reactions always proceed so that the nucleophile or its equivalent, whether an intermolecular species such as an acetate ion, or intramolecular nucleophile such as a migrating group (H-, Me-) or an adjacent bond involved in fragmentation or elimination, becomes associated with the more substituted cationic centre.

C) Protonation and mercuration of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene

In contrast to the mercuration of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) with mercuric acetate in methanol gives 7-exo-acetoxymercurio-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69c; 89 %) resulting from attack at the double bond (Scheme 28). In addition three minor, unidentified, products of 2 %, 1 % and 7 % were also present. The identity of (69c), and in particular the C7-exo stereochemistry of the acetoxymercurio group follows from the ^{13}C-^{199}Hg couplings[87] (Fig. 19) (J ^{13}C-^{199}Hg: C1, 34 Hz; C2, 296 Hz; C3, 68 Hz; C4, not observed; C5, 39 Hz; C6, 136 Hz; C7, 1762 Hz; C8, 17 Hz) and difference NOE spectra (Fig. 20).

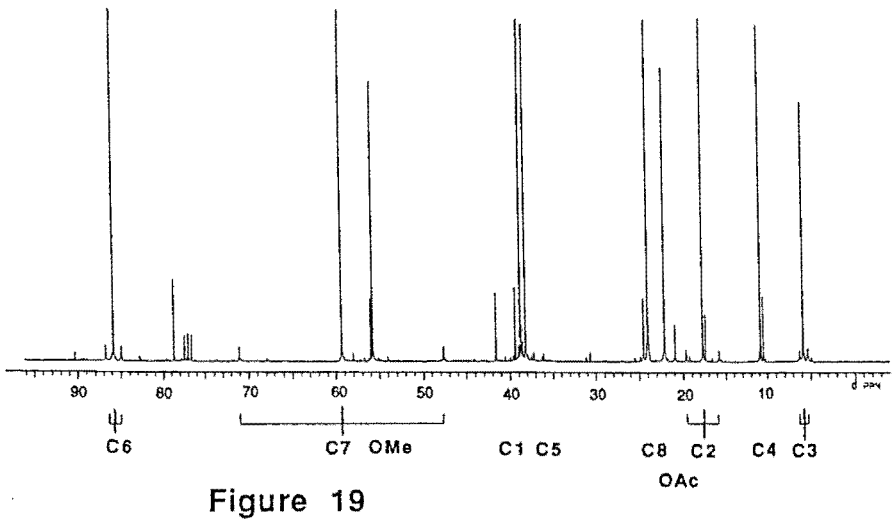
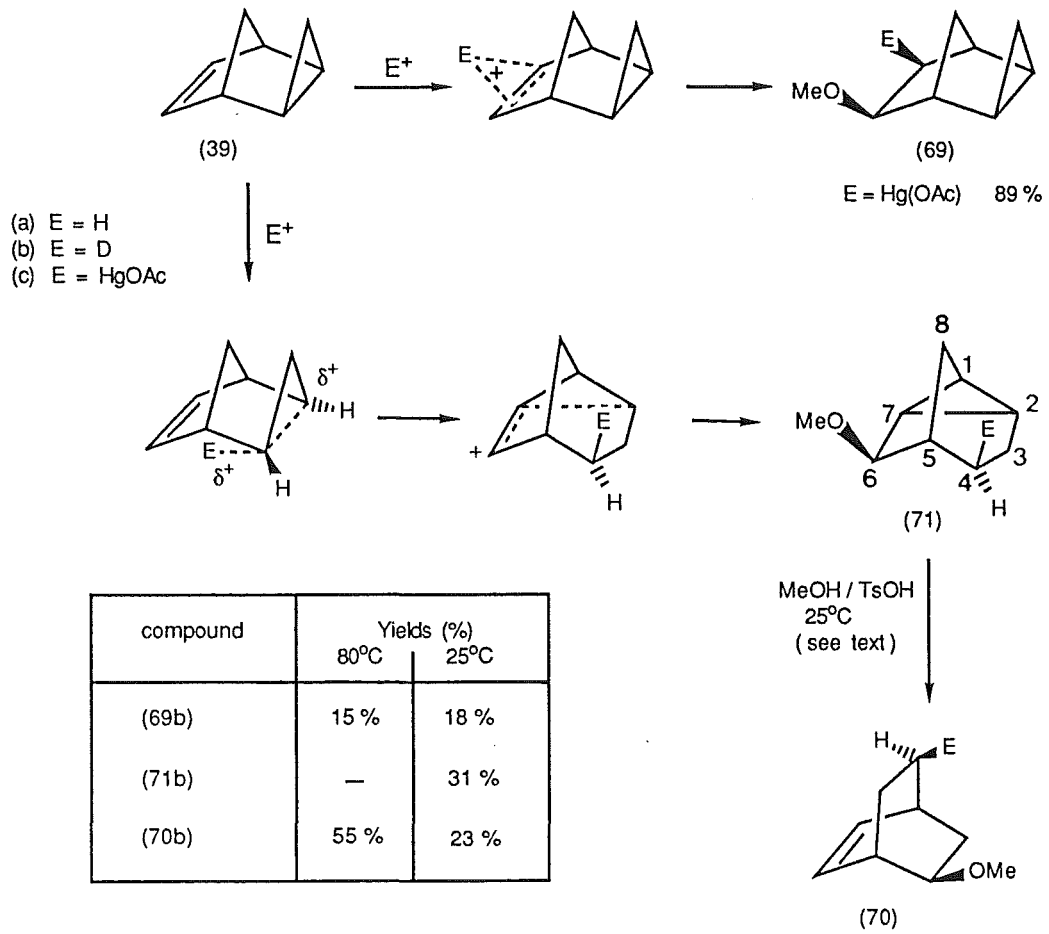


Figure 19

^{13}C nmr of 7-exo-acetoxymercurio-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane showing the ^{13}C - ^{199}Hg coupling.

Irradiation at the C6-endo-H (3.46 ppm) gave enhancements at H7-endo, (2.93 ppm, 9.2 %), H5, (2.55 ppm, 3.2 %) and H4, (0.56 ppm, 7.3 %), consistent with the exo nature of both the



compound	Yields (%) 80°C	25°C
(69b)	15 %	18 %
(71b)	—	31 %
(70b)	55 %	23 %

Scheme 28

Reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with (a) H^+ (D^+) (b) $Hg(OAc)_2$

C6-methoxy and the adjacent C7-acetoxymercurio substituents. A coupling of 6.6 Hz between C6-endo-H and C7-endo-H further confirms the assignment. The similarity between both the ^1H and ^{13}C nmr spectra of (69c) and the analogous exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) in the cyclopropyl region, and in particular the proton-proton couplings and ^{13}C chemical shifts, support the assignment of an exo cyclopropyl group. Further proof was obtained from a difference NOE spectrum; irradiation at H8s (0.89 ppm) giving enhancement at H5, (2.55 ppm, 1.9 %), H1, (2.51 ppm, 2.5 %), H8a, (1.05 ppm, 20.0 %) and H3-exo, (0.68 ppm, 11.1 %).

Reduction of the organomercurial mixture with

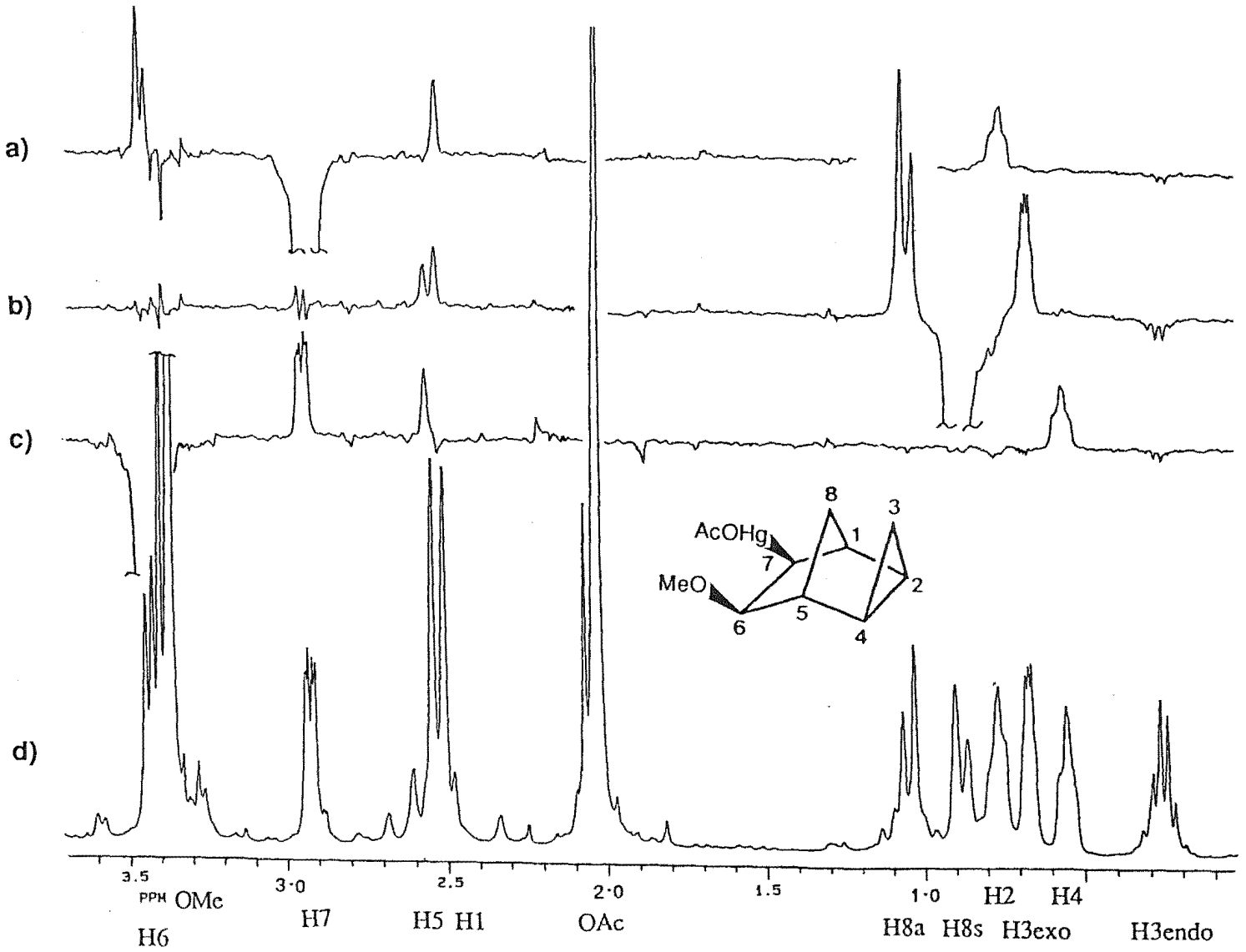


Figure 20

Difference NOE's for 7-exo-acetoxymercurio-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane. Irradiation at a) H7endo b) H8s c) H6endo d) Reference spectrum.

sodium mercury amalgam in sodium hydroxide gave 6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69a). Reduction under these conditions has been shown to proceed with retention of stereochemistry and no rearrangement in related systems.[66] The ^{13}C nmr of (69a) was assigned by comparison with the known exo-tricyclo[3.2.1.$0^{2,4}$]octan-6-exo-ol[88], a heteronuclear correlation spectrum, proton-proton decoupling and difference NOE spectra subsequently allowing complete assignment of the ^{1}H nmr. Stereospecific reduction of the organomercurial product (69c) with sodium mercury amalgam in sodium deuteroxide gave 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b). In contrast, the sodium borodeuteride reduction was less stereospecific, yielding a 73:27 mixture consisting mainly of 7-exo- and 7-endo- deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane respectively.

To determine the reaction pathway in the reaction with proton, and in particular the propensity for rearrangement of the intermediate carbocations, the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) with methanol was studied (Scheme 28). Reaction at 80°C for 7 days yielded 5-exo-methoxybicyclo[2.2.2]oct-2-ene (70a; 55 %) and 6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69a; 15 %) in addition to some high retention (by glc) compounds (30 %). Isolation of the volatile components (69a) and (70a) was achieved by preparative glc.

The identity of 5-exo-methoxybicyclo[2.2.2]oct-2-ene (70a) was determined as follows. The reported ^{1}H nmr[89] was consistent with that observed here. The ^{13}C nmr was assigned by comparison with that of the known bicyclo[2.2.2]oct-2-en-5-exo-ol[90], a heteronuclear correlation experiment subsequently giving the following connectivities: H1, 2.49 ppm / C1, 29.8

ppm; H2, 6.29 ppm / C2, 136.1 ppm; H3, 6.15 ppm / C3, 131.4 ppm; H4, 2.76 ppm / C4, 33.2 ppm; H5-endo, 3.30 ppm / C5, 78.5 ppm; H6-endo 1.73 ppm and H6-exo 1.17 ppm / C6, 33.5 ppm; H7s 1.60 ppm and H7a 1.25 ppm / C7, 25.9 ppm and H8s 1.90 ppm and H8a 1.05 ppm / C8, 17.6 ppm. This established the chemical shifts of the respective protons, but not their configuration and therefore selective decoupling was used to assign the stereochemistry of the $C7H_2$. Irradiation at 3.30 ppm revealed a loss of coupling from H5-endo to H4 (2.78 ppm, J < 2 Hz), H6-endo (1.73 ppm, J 9.7 Hz), H6-exo (1.17 ppm, J 2.5 Hz) and H8a (1.05 ppm, J 1.7 Hz). Similarly, H8a (1.05 ppm) was coupled to H5-endo (3.30 ppm, J 1.7 Hz), H8s (1.90 ppm, J 12.7 Hz), H7s (1.60 ppm, 3.9 Hz) and H7a (1.25 ppm, J 12.0 Hz), thereby establishing the chemical shifts of the C7 methylene protons. Difference NOE's confirmed the above assignments.*

The identity of the second product, 6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69a) was established by comparison with the product obtained from stereospecific sodium mercury amalgam reduction in sodium hydroxide of organomercurial (69c). Their spectral properties were identical in every respect.

To determine the stereochemistry of proton attack in the

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*Footnote: Irradiation at H8s (1.90 ppm) gave enhancements at the OMe, (3.30 ppm, 1.0 %), H4, (2.76 ppm, 2.1 %), H7s, (1.60 ppm, 2.4 %), H7a, (1.25 ppm, 1.4 %) and H8a, (1.05 ppm, 14.4 %). In addition, irradiation at H1 (2.49 ppm) gave enhancements at H2, (6.29 ppm, 2.9 %), H3, (6.15 ppm, 1.0 %), H6endo, (1.73 ppm, ca. 2.6 %), H7s, (1.60 ppm, ca. 1.4 %) and H7a, H6exo, (1.3 - 1.1 ppm, 2.8 % total).

acid catalysed addition, the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) with methanol-d_1 at 80°C was examined. For deuterated (70b), the presence of a triplet at 25.5 ppm in the ^{13}C nmr and a peak at 1.60 ppm in the ^{2}H nmr is consistent with the presence of deuterium at C7-syn. Additional evidence for the deuterium stereochemistry arises from the extensive broadening of H8s at 1.90 ppm, due to the close proximity of the 7-syn deuterium, and the loss of a large coupling from H7-syn to H7-anti at 1.23 ppm. For (69b), the presence of a triplet at 39.8 ppm in the ^{13}C nmr and a peak at 1.30 ppm in the ^{2}H nmr indicates the deuterium is at C7-exo. This compound was identical to the product from stereospecific reduction of organomercurial (69c) in deuterated media.

To accurately determine the preference for proton attack at either the double bond or the cyclopropyl ring, the possibility of further reaction at the cyclopropyl ring of (69a) was examined. It would be expected that, given the greater rate of proton attack at an isolated cyclopropyl ring as compared with a double bond, (69a) would be attacked in preference to (70a). A sample of 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b), obtained from sodium mercury amalgam reduction of (69c) in deuterated media, was heated at 80°C in methanol, p-toluenesulphonic acid for 7 days, the same conditions as the primary reaction was carried out. Glc analysis at the end of this time revealed the presence of starting material (69b; 52 %) and high retention compounds (35 %). The non volatile compounds observed arise from subsequent reaction of (69a/b) with methanol to yield more polar di-methoxy products, and therefore the 15 % of 6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69) obtained from reaction of proton (deuteron) with exo-tricyclo[3.2.1.$0^{2,4}$]-

oct-6-ene (39) must be regarded as a minimum.

The presence of a 7-syn-deuterium in (70b) is consistent with initial attack by a proton (deuteron) at C2 (C4) with inversion of stereochemistry, subsequent W-M rearrangement giving the bicyclo[2.2.2]oct-2-ene system. However, such a rearrangement is unexpected in view of the significant overlap between the C2,C4 carbons on the cyclopropyl ring with the pi system.[70a,83] A more probable primary reaction product is 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71), formed from interaction of the C2,C4 orbitals with the pi orbitals. This compound would be expected to be unstable under the reaction conditions employed, subsequently solvolysing to 5-exo-methoxybicyclo[2.2.2]oct-2-ene. Such behaviour is found in the solvolysis of tricyclo[3.2.1.$0^{2,7}$]octan-6-exo (and endo) -ol, acetolysis of a mixture of the two epimeric alcohols at room temperature quantitatively yielding bicyclo[2.2.2]oct-2-en-5-exo-ol.[91] To determine if a similar product is indeed an intermediate, the acid catalysed reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene was carried out at room temperature in order to trap any such products that are unstable at higher temperatures. Reaction of (39) for 28 days gave (Scheme 28) the previously observed 6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69a, 18 %) in addition to 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71a, 31 %), 5-exo-methoxybicylo[2.2.2]oct-2-ene (70a; 23 %), unreacted exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39, 23 %) and unidentified compounds (3 % and 2 %). Separation was achieved by preparative glc.

The identity of (71a) was determined as follows. Difference NOE spectra showed that irradiation at H6-endo (3.52 ppm) gave enhancement at the methoxy methyl (3.34

ppm, 1.2 %), H5 (1.96 ppm, 1.3 %), H3-endo (ca. 1.74 ppm, 0.8 %), H7 (1.51 ppm, 1.1 %) and H4-endo (1.32 ppm, 2.3 %). Further, irradiation at H2 (0.92 ppm) gave enhancements at H3-exo and H3-endo (1.7 % total), H7 (ca. 3.4 %) and H1 (ca. 5.7 %). The configuration of the C6-H was established as endo from its presence as a singlet in the ^{1}H nmr, this being similar to the corresponding 2-methyltricyclo[3.2.1.$0^{2,7}$]-octan-6-exo-ol[92a] and tricyclo[3.2.1.$0^{2,7}$]octan-6-exo-ol.[91,92b] The C2-H at 0.92 ppm was assigned from the previously mentioned NOE and also from the coupling with H3-exo and H3-endo (ca. 1.75 ppm, J = 2.7 Hz each), H7 (1.51 ppm, 8.0 Hz) and H1 (1.41 ppm, 8.0 Hz). This is consistent with the presence of an endocyclic cyclopropyl proton adjacent to the C3 methylene at 1.75 ppm. To establish the stereochemistry of deuteron attack at the cyclopropyl ring, it was necessary to unambiguously determine the chemical shifts of the C4-exo-H and the C4-endo-H. Assignment of the 4-endo proton at 1.32 ppm follows from an NOE with H6-endo (2.3 %) and coupling with H8a at 1.88 ppm (2.2 Hz), H8a being assigned from its coupling with H5 (1.96 ppm, 5.7 Hz), H8s (1.51 ppm, 11.4 Hz) and H1 (1.40 ppm, 3.4 Hz), in addition to its' coupling with H4-endo. A heteronuclear correlation spectrum allowed assignment of the carbon-hydrogen connectivities and in particular, those of H4-exo 1.58 ppm and H4-endo 1.32 ppm / C4, 26.5 ppm.

The acid catalysed reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) in methanol-d_1 at room temperature gave after 72 days (74 % reaction) 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b), 7-syn-deutero-5-exo-methoxybicyclo[2.2.2]oct-2-ene (70b) and 4-exo-deutero-6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane

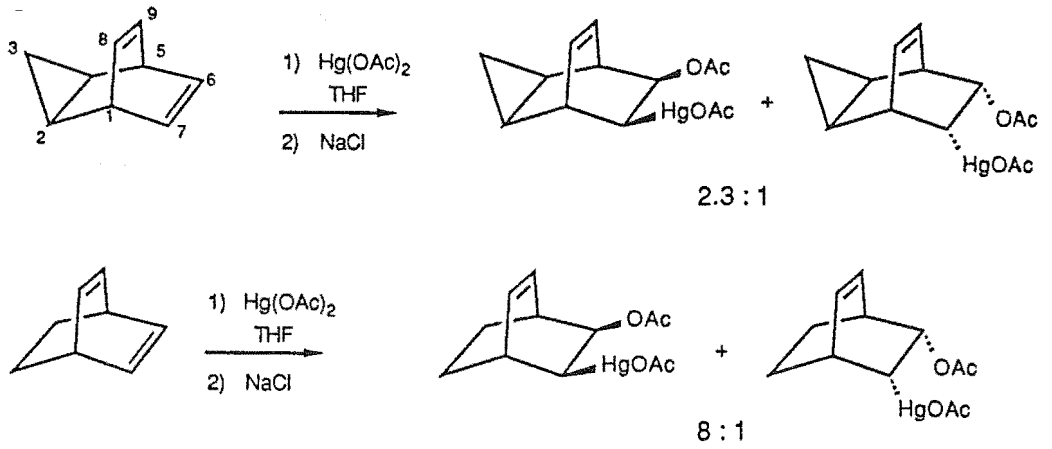
(71b). For (71b), the presence of a triplet in the ^{13}C nmr at 26.1 ppm and a peak in the ^{2}H nmr at 1.52 ppm identifies the deuterium as being at C4-exo, consistent with proton (deuteron) attack at C2 (C4) of the cyclopropane ring occurring with inversion. Both (69b) and (70b) obtained from this reaction were identical with isolated samples obtained from the reaction with methanol-d_1 at 80°C and previously discussed.

The stability of (71a) was examined by stirring it at room temperature in methanol, p-toluenesulphonic acid and following the reaction by glc. Approximately 2 hours after the start of the reaction, glc analysis showed the mixture to contain (71a; 55 %) in addition to the bicyclic [2.2.2]oct-2-ene (70a), this product ratio remaining invariant for 16 days. Therefore, the presence of (70a) demonstrated that it arises from (71a) in the reaction at both 25°C and 80°C.

The absence of rearranged product from the proton attack at the double bond in both reaction at 80°C and room temperature is notable. Such a situation is also found in the acetolysis of bicyclo[2.2.1]hepta-2,5-diene with added methanol[93], where rearrangement to the tricyclo[2.2.1.$0^{2,6}$]heptane skeleton accounts for approximately 30 % of the reaction of acetic acid. However, rearranged product accounts for only 13 % for the reaction with methanol, unrearranged 5-exo-methoxybicyclo[2.2.1]hept-2-ene comprising the remaining 87 %. Given the smaller orbital overlap between the cyclopropyl ring and pi system in hydrocarbon (39) than that of the pi system for norbornadiene[83] the absence of rearrangement is expected in the methanolysis of (39). When

the reaction is effected with stronger acids rearrangement would be expected to become increasingly important.[93]

For the mercuration of both exo-tricyclo[3.2.1.$0^{2,4}$]oct-



Scheme 29

Oxymercuration of tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene. The corresponding reaction with bicyclo[2.2.2]octa-2,5-diene is shown for comparison.

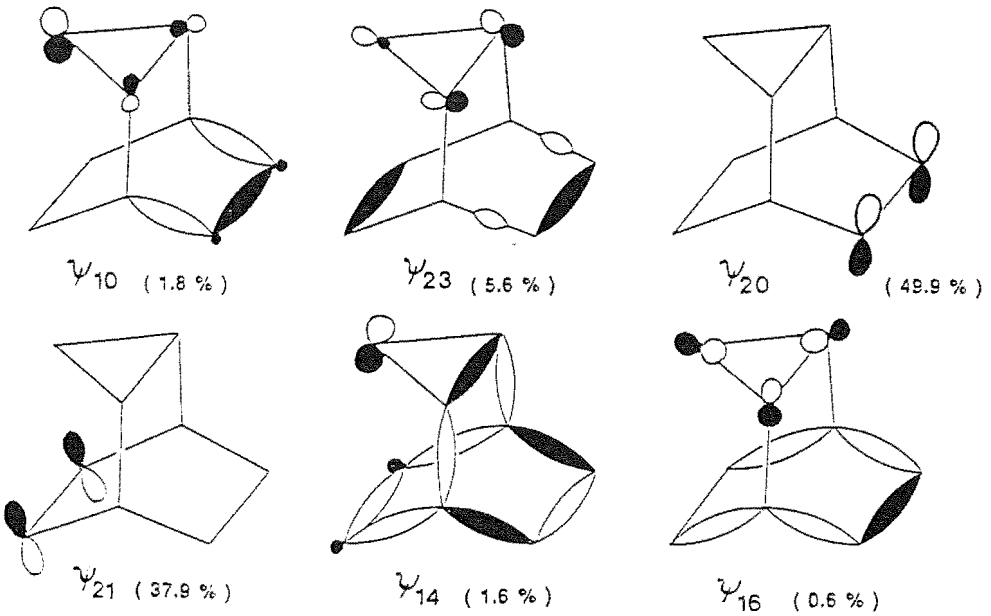


Figure 21

Relative contributions of the precanonical molecular orbitals to the 15a' HOMO of tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene.

6-ene and tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene[94] (Scheme 29), predominant attack at the double bond has been observed. For tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene, a consideration of the theoretically calculated orbital contributions to the 15a' HOMO (Fig. 21)[79] allows such a preference to be rationalised. The significant contribution of the Ψ_{20} precanonical molecular orbital to the HOMO is a result of the significant through space interaction between the cyclopropyl orbitals and the C6,C7 pi orbitals. Such an interaction is reflected by the large overlap integral $<\pi|\sigma_s>$ of 0.061 for the analogous exo-tricyclo[3.2.2.$0^{2,4}$]oct-6-ene.[83] Comparative values of overlap integrals for exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, where such an interaction is present but of reduced magnitude, and endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, where a cyclopropyl/double bond interaction is absent are 0.052 and 0.012 respectively.[83]

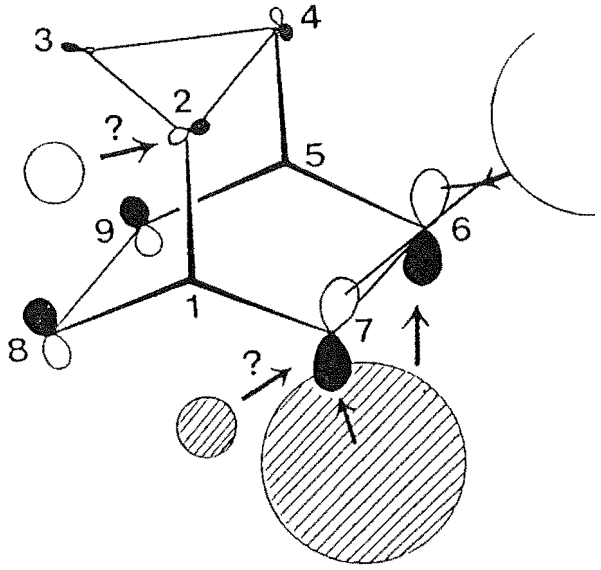


Figure 22

The main features of the 15a' HOMO of tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene showing attack by mercuric acetate (and proposed attack by proton).

A pictorial representation of the important features of the 15a' HOMO in tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene is shown (Fig. 22). Since the intermediate carbocation stabilities from

mercuric acetate attack at a cyclopropane or double bond are comparable in the absence of any external stabilisation mechanism (Chapter 2), and given the low degree of charge development usually observed in oxymercurations, orbital interactions of the type shown in Fig. 22 determine the reaction pathway. A favourable overlap between the mercury LUMO and the C6,C7 component of the hydrocarbon HOMO therefore favours attack at the C6,C7 pi system to the exclusion of the C8,C9 pi bond and the cyclopropyl ring.

For exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene the corresponding HOMO (Fig. 23) will differ from that shown in Figure 22 in that there is only a single pi orbital. More importantly, the

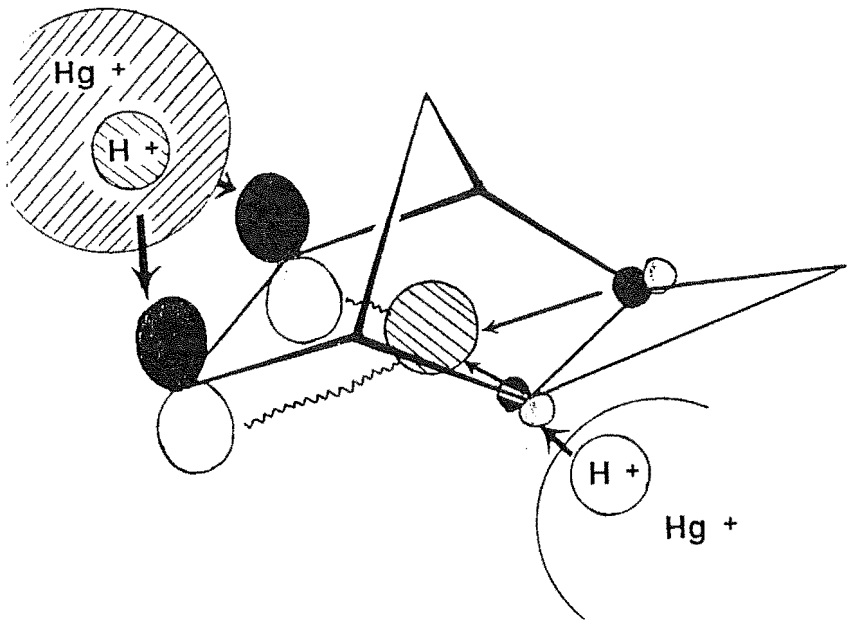


Figure 23

Proposed HOMO in exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene showing the hydrocarbon HOMO / electrophile LUMO interaction.

cyclopropyl contribution to the HOMO will be larger, a result of a decrease in the through space interaction between the cyclopropyl orbitals and the pi orbitals relative to that in tricyclo[3.2.2.$0^{2,4}$]nona-6,8-diene. Such a decrease in orbital interaction will result in a decrease in the HOMO-e_s energy difference, and consequently result in a greater degree of

cyclopropyl e_s bond character in the HOMO (Fig. 24). In the reaction of hydrocarbon (39) with mercuric acetate, the most favourable orbital overlap is still at the pi system. However, an increase in the cyclopropyl contribution to the HOMO

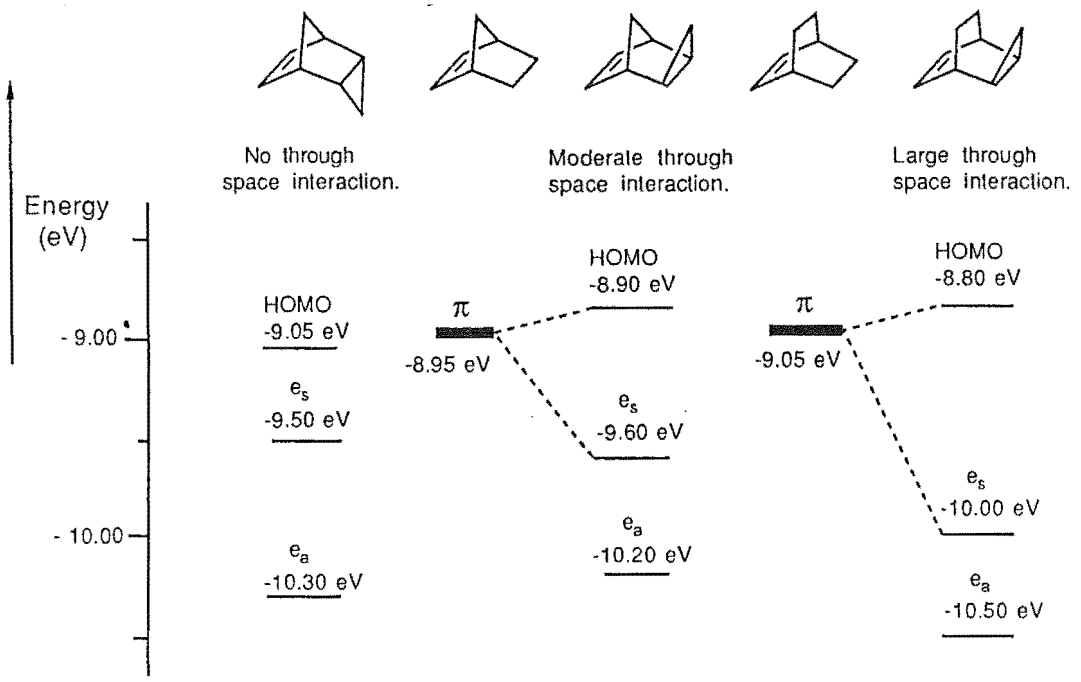


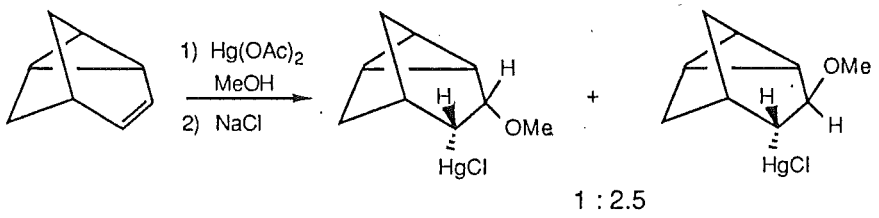
Figure 24

The result of through space interactions on orbital energies as revealed by photoelectron spectroscopy.

allows cyclopropyl attack (ca. 11 %) to compete with attack at the double bond. In the reaction of hydrocarbon (39) with proton, orbital overlap is more favourable at the double bond than the cyclopropyl ring. However, since attack at the cyclopropyl ring is kinetically faster than attack at a double bond (Chapter 2), cyclopropyl ring cleavage is more favoured than attack at the double bond. This is reflected by the relative ratios of (69a) to [(70a) + (71a)] as being 18:54 respectively in the reaction at room temperature. The cleavage of the cyclopropyl ring at C2,C4 results from the high contribution of the 3e'(S) orbital to the HOMO and the large HOMO-e_a separation. Further, since edge attack at this bond is

disfavoured due to an unfavourable secondary orbital interaction with the pi component of the HOMO (Figure 23), corner attack at C2 (C4) results.

A through bond interaction between the cyclopropane orbitals and the pi system would be expected to similarly result in a raising of the HOMO, and an increase in its pi contribution at the expense of the cyclopropyl component. Such is the situation in the oxymercuration of tricyclo[3.2.1.$0^{2,7}$]oct-3-ene[94], where only products from double bond attack were reported (Scheme 30).



Scheme 30

Oxymercuration of tricyclo[3.2.1.$0^{2,7}$]oct-3-ene.

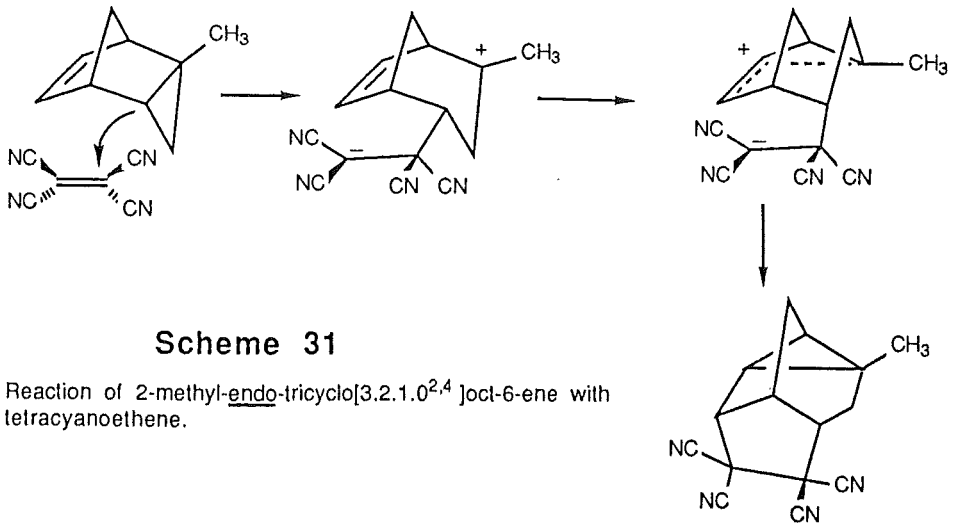
The observation of mercuric acetate attack at the position β to the cyclopropyl group reflects an increase in the orbital size at this position in the pi bond upon substitution with a conjugating group.[95] Carbocation stabilities do not determine the reaction pathway to any great extent, as shown by the lack of rearranged products observed.

Chapter 4

A) Introduction

To determine the effect a methyl substituent has on the reaction pathway for electrophilic addition to a cyclopropyl ring, the methanol and mercuric acetate additions to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) and 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) were examined. In view of the lower stability of the expected tertiary methoxy product(s) from the acid catalysed methanol additions, the reactions were carried out at 25°C.

The addition of a methyl substituent has a marked effect on the reaction pathway in the tetracyanoethene addition to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) as compared with endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37). For the reaction of (37) with tetracyanoethene[69], the product results from intramolecular nucleophilic attack at the allylic positive charge, formed from the intermediary bridged species resulting from interaction of the C1-C8 and C5-C8 sigma orbitals and the positive charge at C2 (Scheme 22).



Scheme 31

Reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with tetracyanoethene.

However the intermediate formed in the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[78] (38) with tetracyanoethene is stable enough to allow conformational inversion at C3 and subsequent interaction of the positive charge at C2 with the pi system (Scheme 31). Thus, it would be expected that the additional methyl group present in 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (-6-ene; 38) would bring dramatic changes in the reaction pathway of these compounds with methanol or mercuric acetate as compared with the analogous endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) (-6-ene; 37).

B) Protonation and mercuration of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane

Reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with a catalytic amount of p-toluenesulphonic acid in methanol at 25°C for 4 days gave (Scheme 32) 2-methylbicyclo[3.2.1]-oct-2-ene (74a; 18 %), 2-exo-methoxy-2-endo-methylbicyclo-[3.2.1]octane (73a; 32 %) and 2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]octane (72a; 31 %), the remainder being unreacted starting material. Separation was achieved by preparative glc.

The identity of 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]-octane (72a) was determined as follows. The ^{13}C nmr was assigned by comparison with the reported spectrum* of 2-exo-methylbicyclo[3.2.1]octan-2-endo-ol[64], and a

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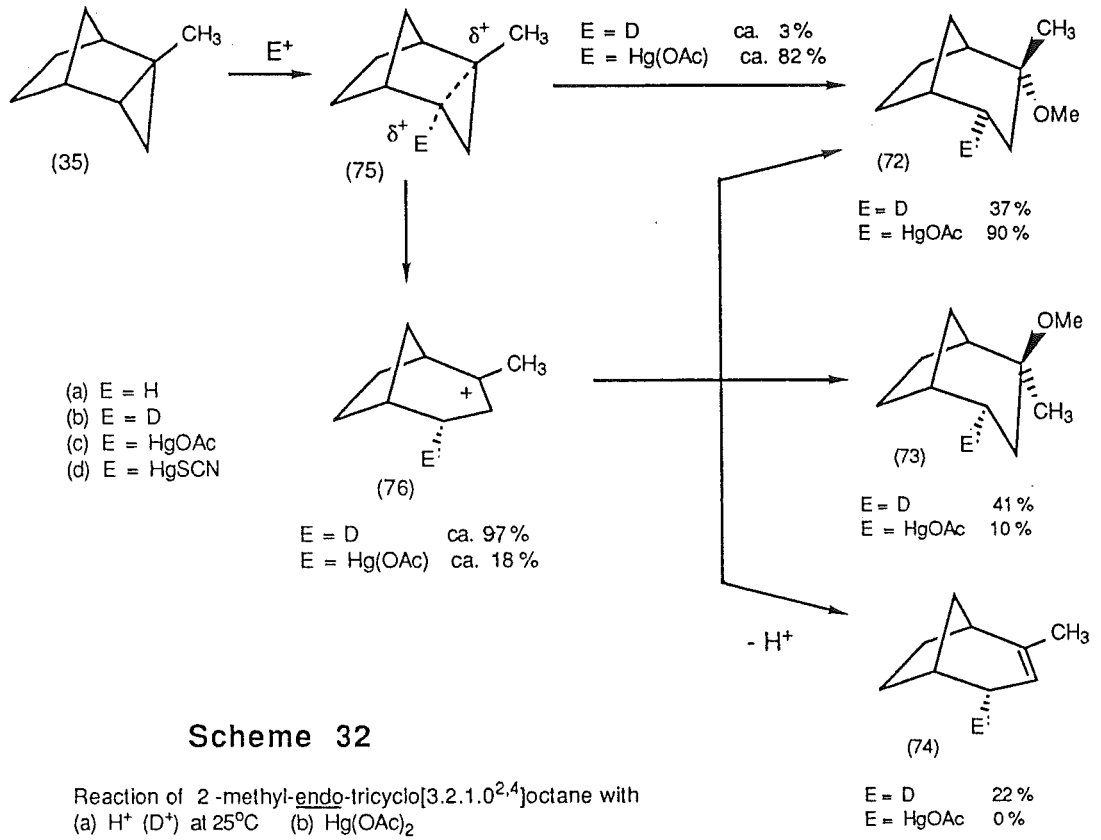
*Footnote: The previously reported assignments for C3 and C4 are subsequently shown to be incorrect.

heteronuclear correlation experiment established the following connectivities: H1, 2.13 ppm / C1, 42.9 ppm; H3-exo and H3-endo 1.55 - 1.45 ppm / C3, 31.4 ppm; H4-exo and H4-endo 1.43 ppm / C4, 30.0 ppm; H5, 2.13 ppm / C5, 34.5 ppm; H6-exo 1.65 ppm and H6-endo 1.43 ppm / C6, 27.6 ppm; H7-exo 1.84 ppm and H7-endo 1.51 ppm / C7, 24.5 ppm and H8a 1.56 ppm and H8s 1.28 ppm / C8, 35.5 ppm. A difference NOE

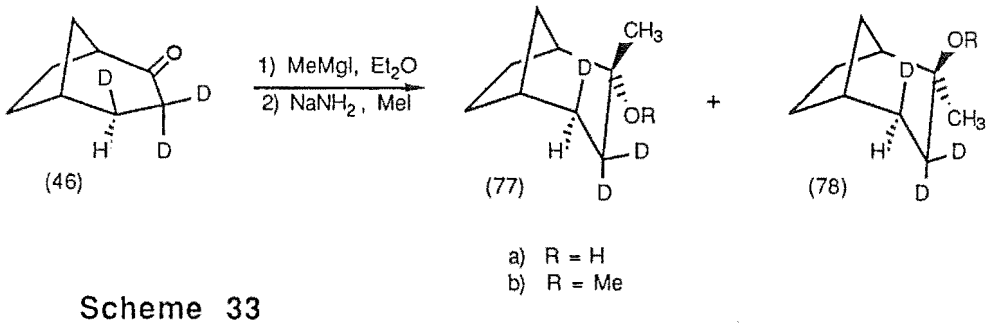


Scheme 32

Reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane with (a) H^+ (D^+) at 25°C (b) $Hg(OAc)_2$

spectrum showed that irradiation of the methyl at 1.20 ppm gave enhancements at 3.17 ppm (OMe), 2.15 ppm (H1, 3.2 %), 1.28 ppm (H8s, 3.3 %) and 1.45 ppm (H4-exo, 2.6 %) thereby establishing the exo stereochemistry of the methyl. The ^{13}C nmr of 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) was assigned by comparison with the known 2-endo-methylbicyclo-[3.2.1]octan-2-exo-ol[64], and a heteronuclear correlation experiment allowed assignment of the chemical shifts of the protons.

To determine the reaction pathway for the acid catalysed methanol addition to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35), the chemical shifts of the 4-exo and 4-endo protons for each of the primary reaction products (72a), (73a) and (74a) had to be unambiguously assigned. To achieve this, authentic deutero isomers (77b) and (78b) of the epimeric 2-methoxy-2-methylbicyclo[3.2.1]octanes were synthesized (Scheme 33). The previously prepared 3,3,4-exo-trideutero-bicyclo[3.2.1]octan-2-one (46; Chapter 2) was reacted with methyl magnesium iodide to give a 66:34 mixture of 2-exo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-endo-ol (77a) and 2-endo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]-octan-2-exo-ol (78a).[96]



Scheme 33

Preparation of the epimeric 3,3,4-exo-trideutero-2-methoxy-2-methylbicyclo[3.2.1]octanes.

The previously reported ^{13}C nmr assignments for C3 and C4 of 2-exo-methylbicyclo[3.2.1]octan-2-endo-ol[64] are required to be reversed, as shown by the presence of a triplet at 29.6 ppm from the C4 deuterium and apparent absence of a peak at 33.7 ppm due to D3-exo,D3-endo in 2-exo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-endo-ol (77a). The mixture of alcohols was methylated by sodium amide, methyl iodide and a heteronuclear correlation spectrum run of the crude, epimeric 2-methoxy-2-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octanes (77b) and (78b). For the trideuterated methoxy ether (77b), a triplet in the carbon dimension was observed at 29.4 ppm,

exhibiting connectivity with a proton at 1.42 ppm. The presence of a triplet in the carbon dimension arises from the C4-exo-D coupling, C4 exhibiting connectivity with only H4-endo at 1.42 ppm due to the high deuterium incorporation at C4-exo. Thus, the chemical shift of H4-endo in (72a) is established as 1.42 ppm, coincident with H4-exo.* For 2-exo-methoxy-2-endo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]-octane (78b), the heteronuclear correlation spectrum showed a triplet in the carbon dimension at 28.3 ppm, exhibiting connectivity with H4-endo at 1.21 ppm. As with (77b), the triplet in the carbon dimension arises from the C4-exo-D coupling, no connectivity being observed between C4 and H4-exo due to the high deuterium incorporation at this position. Thus, for 2-exo-methoxy-2-endo-methylbicyclo-[3.2.1]octane (73a), the chemical shifts of H4-endo and H4-exo are established as 1.21 ppm and 1.65 ppm respectively.

The identity of 2-methylbicyclo[3.2.1]oct-2-ene (74a) followed by comparison with the reported ^{13}C nmr[64], and by preparation of authentic material. The mixture of epimeric 2-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-ol's (77a) and (78a) was dehydrated by heating with $KHSO_4$ at 160°C for 30 minutes[97] to yield 2-methylbicyclo[3.2.1]oct-2-ene, with deuterium present at C3 (5.05 ppm, 25 %), C4-exo (2.30 ppm, 53 %), C4-endo (1.75 ppm, 29 %) and the methyl (1.65 ppm, 0.40

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*Footnote: A ^2H nmr spectrum of 4-exo- and 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane, prepared from the non stereospecific $NaBD_4$ reduction (Chapter 2) of 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]octane, showed a single peak at 1.41 ppm due to D4-exo and D4-endo.

excess deuterium). A heteronuclear correlation spectrum of this compound shows in the carbon dimension, a triplet at 36.5 ppm exhibiting connectivity with H4-endo at 1.75 ppm, no connectivity with H4-exo being observed due to the higher deuterium incorporation at this position. Hence, for 2-methylbicyclo[3.2.1]oct-2-ene (74a), the chemical shifts of H4-exo and H4-endo are established as 2.30 ppm and 1.75 ppm respectively.

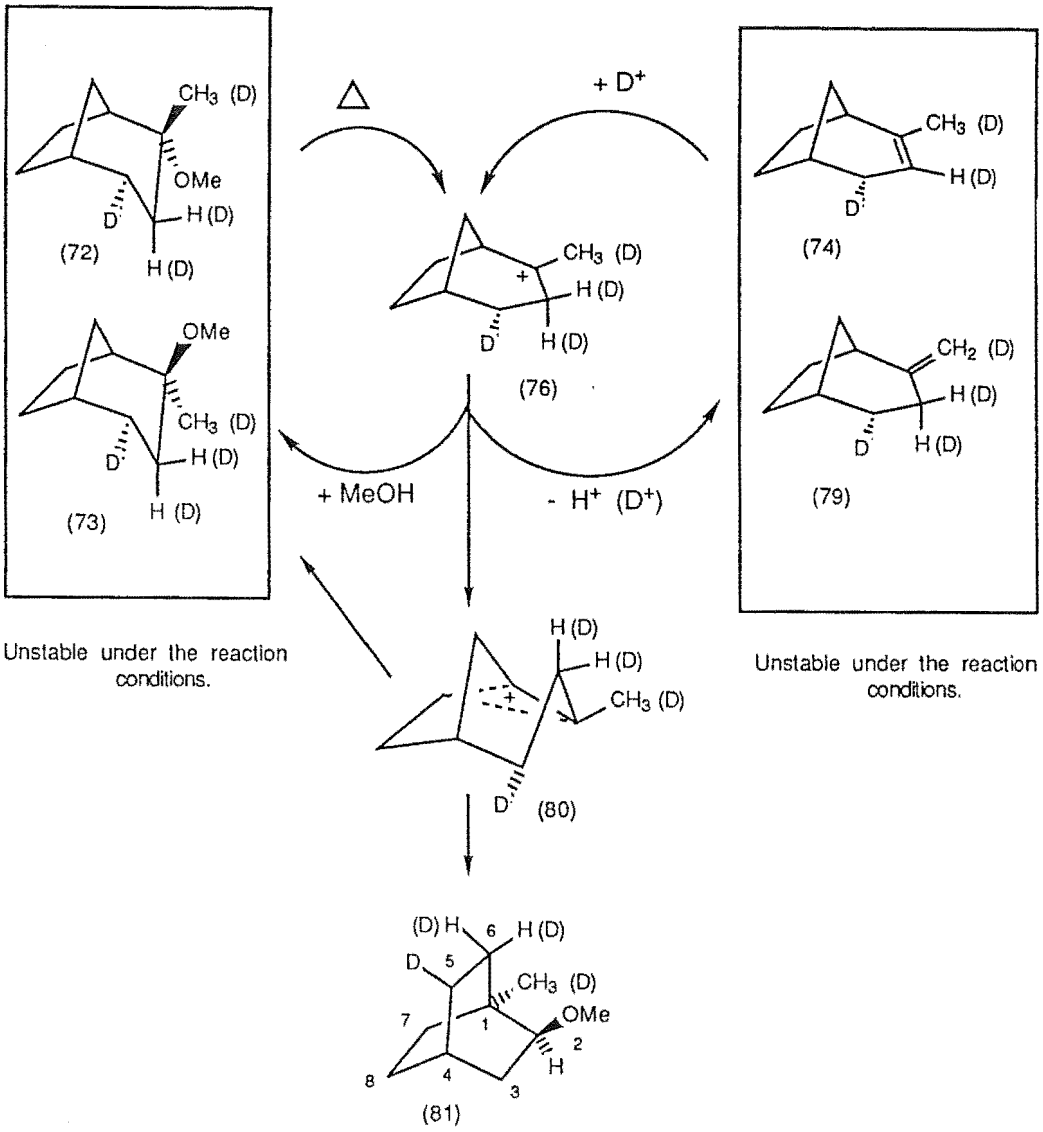
The stability of 2-exo-methoxy-2-endo-methylbicyclo-[3.2.1]octane (73a) and 2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (72a) towards the reaction conditions was established by stirring separate samples in methanol, p-toluenesulphonic acid at room temperature and monitoring by glc. No rearrangement was observed after 21 days, thus indicating the epimeric pair of methoxy ethers (72a) and (73a) are kinetic in origin, as is the alkene (74a).

In contrast to the acid catalysed addition reaction, the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane with mercuric acetate in methanol yields, after sodium mercury amalgam reduction in sodium hydroxide, a 9:1 mixture of 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) and 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) respectively. Separation was achieved by preparative glc and the products were identical to those from the acid catalysed methanol addition at room temperature. While the intermediate organomercurial mixture was not separated, the major component of this reaction, 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72c), was present in sufficient quantity to allow the determination of its spectroscopic data. The ^{13}C-^{199}Hg couplings (J ^{13}C-^{199}Hg: C1, 27 Hz; C2, ca. 284 Hz; C3, 67 Hz; C4, 1662 Hz; C5, 74 Hz; C6,

28 Hz; C7, not obs.; C8, 255 Hz), are consistent with a 4-endo-acetoxymercurio group (Chapter 2). The axial nature of the C4-H, and hence the configuration of the acetoxymercurio group in (72c) was further confirmed by proton-proton couplings (selective decoupling) to C3-endo-H (13.6 Hz), C3-exo-H (5.2 Hz), C6-exo-H (1.5 Hz) and C5H (1.5 Hz). A difference NOE spectrum, performed on the mixture (9:1) of the thiocyanatomercurials (72d) and (73d), showed that irradiation of the methyl group at 1.20 ppm gave enhancements at 3.18 ppm (OMe, 5.1 %), 2.91 ppm (H4-exo, 5.6 %), 2.07 ppm (H1, 2.8 %), 1.96 ppm (H3-exo, 3.2 %) and 1.56 ppm (H8s, 3.5 %) thereby confirming the exo stereochemistry of the methyl and hence the endo nature of the methoxy group. Reduction of the organomercurial mixture with sodium mercury amalgam in sodium deuteroxide gave a 93:7 mixture of 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b) and 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b). The observation of C4-endo deuterium in the minor reduction product (73b) and a 4-endo-acetoxymercurio group in the major organomercurial product (72c) requires corner attack by the mercuric acetate without skeletal rearrangement.

To observe the effect of temperature on the reaction course, ie: the preference for thermodynamic control vs. kinetic control, 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane was reacted with methanol p-toluenesulphonic acid at 80°C for 7 days. Glc analysis of the products revealed the presence of the previously observed 2-methylbicyclo[3.2.1]oct-2-ene (74a; 53 %), 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a; 18 %) and 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a; 21 %), in addition to another compound subsequently identified as 2-methoxy-1-methylbicyclo[2.2.2]octane (81a; 8 %). Isolation

was achieved by preparative glc. The partial ^{1}H nmr of 2-methoxy-1-methylbicyclo[2.2.2]octane has been reported[98], and is consistent with that observed here.* The coupling data (selective decoupling) showed coupling from H2-endo at 3.02 ppm to H3-endo (1.84 ppm, 9.0 Hz), H3-exo (1.49 ppm, 3.5 Hz) and



Scheme 34

Rearrangement of the products from the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane in methanol-d_1 at 80 °C.

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*Footnote: the ^{13}C nmr was assigned from the predicted effect of a methoxy group on the ^{13}C nmr of 1-methylbicyclo[2.2.2]-octane.[99]

H6a (1.08 ppm, 1.7 Hz). H3-endo was additionally coupled to H3-exo (12.4 Hz), H4 (1.64 ppm, 2.9 Hz) and H5a (1.46 ppm, 2.9 Hz), thereby allowing assignment of H5a. A heteronuclear correlation experiment gave the following connectivities: H2, 3.02 ppm / C2, 82.8 ppm; H3-exo 1.49 ppm and H3-endo 1.84 ppm / C3, 34.5 ppm; H4, 1.64 ppm / C4, 24.8 ppm; H5a 1.46 ppm and H5s 1.54 ppm / C5, 26.0 ppm; H6a 1.08 ppm and H6s 1.64 ppm / C6, 26.2 ppm; H7exo 1.43 ppm and H7endo 1.28 ppm / C7, 32.1 ppm; H8exo 1.51 ppm and H8endo 1.41 ppm / C8, 25.6 ppm and methyl, 0.83 ppm / CH_3, 24.7 ppm. This allowed assignment of H6s and H5s at 1.64 ppm and 1.54 ppm respectively.

The stability of the primary reaction products from the reaction at room temperature under the more vigorous conditions was determined by separately reacting each of the compounds in methanol p-toluenesulphonic acid at 80°C. The results are shown in Table 10.

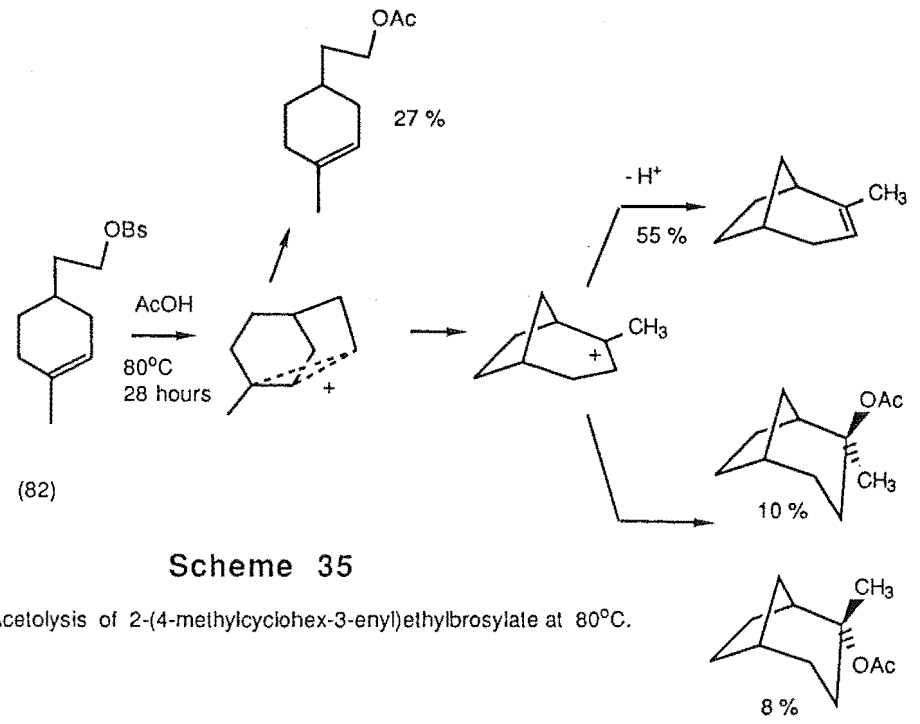
Reactant	Product distribution (ratios) (74a)	(81a)	(72a)	(73a)	Reaction time	[H+] (M)
(72a) : (73a) (9 : 1)	92 67	— 16	4 8	2 9	26 hours 8 days	0.115 0.115
(72a) : (73a) (32 : 68)	23 69	7 16	34 8	36 8	25 hours 8 days	0.115 0.115
(74a)	28	2	36	34	8 days	0.01

Table 10

Stability of the primary reaction products to methanol p-toluenesulphonic acid at 80°C.

It is readily apparent that these compounds are not stable under these conditions and that with time the product of thermodynamic control, 2-methoxy-1-methylbicyclo[2.2.2]octane (81a), begins to increase in abundance (Scheme 34).

The acetolysis of 2-(4-methylcyclohex-3-enyl)ethyl brosylate[100] (82) at 80°C for 28 hours has been reported to yield 2-methylbicyclo[3.2.1]oct-2-ene (55 %), 2-endo-acetoxy-2-exo-methylbicyclo[3.2.1]octane (8 %), 2-exo-acetoxy-2-endo-methylbicyclo[3.2.1]octane (10 %) and 2-(4-methylcyclohex-3-enyl)ethyl acetate (27 %) (Scheme 35).



Scheme 35

Acetolysis of 2-(4-methylcyclohex-3-enyl)ethylbrosylate at 80°C.

These products were similarly unstable under the reaction conditions employed. Comparison by glc with authentic compound discounted the presence of 2-acetoxy-1-methylbicyclo[2.2.2]-octane. However, such results are not inconsistent with those observed in the acid catalysed methanol addition to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (Table 10), since 2-methoxy-1-methylbicyclo[2.2.2]octane (81a) appears only after prolonged periods at 80°C. Leakage from the tertiary cation (76) to cation (80) and subsequent nucleophilic attack will give the bicyclo[2.2.2]octane (81) (Scheme 34).[101]

To determine the stereochemistry of proton attack, the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with

methanol-d_1, p-toluenesulphonic acid was examined at 25°C and the products separated by preparative glc. For deuterated (74b), the presence of a triplet in the ^{13}C nmr spectrum at 36.3 ppm and a peak in the ^{2}H nmr at 1.75 ppm indicates the deuterium stereochemistry at C4 as being endo. For 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b), the presence of a triplet in the ^{13}C nmr at 28.6 ppm and a peak in the ^{2}H nmr at 1.23 ppm similarly indicates the deuterium stereochemistry at C4 in this compound as being endo. However while the ^{13}C nmr for 2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (72b) indicates the presence of C4-D due to the presence of a triplet at 29.7 ppm, the unfortunate coincidence of the chemical shifts of the 4-exo and 4-endo protons (and hence deuterons), means the deuterium stereochemistry at C4 is indeterminate.

To ascertain the stereochemistry of C4-D in (72b), a 76:24 mixture of 4-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]-octane (72b) and 4-endo-deutero-2-exo-methoxy-2-endo-methyl-bicyclo[3.2.1]octane (73b), obtained by preparative glc from the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with methanol-d_1 at room temperature, was reacted with methanol, p-toluenesulphonic acid at 80°C for 32 hours. Glc, and subsequent ^{1}H, ^{2}H and ^{13}C nmr analyses confirmed the presence of 4-endo-deutero-2-methylbicyclo[3.2.1]oct-2-ene (74b; 57 %), 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (73b; 19 %) and 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (72b; 23 %). The presence of triplets in the ^{13}C nmr of the crude reaction mixture corresponding to C4-D for each of (72b), (73b) and (74b), and the presence of peaks in the ^{2}H nmr at 1.72 ppm (74b), 1.40 ppm

(72b) and 1.23 ppm (73b) along with the absence of peaks corresponding to 4-exo-deutero-2-methylbicyclo[3.2.1]oct-3-ene (2.27 ppm) and 4-exo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (1.62 ppm) indicates the deuterium stereochemistry at C4 in 4-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b) as being endo. Resolution of the 4-exo and 4-endo deuterons in the product from non stereospecific $NaBD_4$ reduction of 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane by the use of $Eu(fod)_3$ shift reagent was attempted, but was unsuccessful.

The observation of C4-endo-D in all three of the primary reaction products from the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with methanol-d_1 at room temperature is consistent with corner attack by proton (deuteron) at the cyclopropyl ring. This reflects either (i) an inherent preference for protonation at C4 as compared with C3 or (ii) subsequent reaction at the C4 protonated cation is more facile than reaction at the C3 protonated cation. In a manner similar to endo-tricyclo[3.2.1.$0^{2,4}$]octane (34), the HOMO* of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane will contain a contribution from the C1,C8 / C5,C8 sigma bonds (Chapter 2). An unfavourable secondary orbital interaction with the C2,C4 edge protonated species disfavours edge attack and favours corner attack at C4. For attack by mercuric acetate the

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*Footnote: In the absence of any theoretical or experimental orbital studies on 1,1,2-trisubstituted cyclopropanes it must be assumed that, by analogy with endo-tricyclo-[3.2.1.$0^{2,4}$]octane, the HOMO will contain a contribution from the Walsh e_s orbital.

preference for corner attack at C4 reflects the favourable cyclopropyl HOMO/mercury LUMO interaction. Edge attack at C2,C4 of the cyclopropyl ring is disfavoured due to an unfavourable secondary orbital interaction with the C1,C8/C5,C8 contribution to the HOMO. Corner attack at C4 is therefore favoured due to the absence of any such interactions. The lack of rearranged products resulting from C1,C8 sigma bond interaction with the positive charge at C2 indicates electron donation from the C1,C8 bond is no longer necessary. The methyl group is now able to satisfy the bulk of the electronic demand in polarisation of the cyclopropyl group upon protonation. The lack of stereospecifity observed in nucleophilic attack in this system, as represented by the ratio of (72a:73a), cannot be explained by the intermediacy of the cation (75) alone. However, the results can be accommodated by inclusion of the free tertiary carbocation (76) as an intermediate in competition with the bridged species (75). Solvolysis of the p-nitrobenzoate of 1-methylbicyclo[2.2.2]octan-2-ol in either acetone / water or acetic acid* gave only 2-exo-methylbicyclo[3.2.1]octan-2-endo-ol (45 %) and 2-endo-methylbicyclo[3.2.1]octan-2-exo-ol (55 %), the products from kinetic attack at the 2-methylbicyclo[3.2.1]octan-2-yl cation (76).[102] Assuming methanol attack on (76) proceeds with a similar ratio, then the product ratios observed in the acid catalysed methanol addition of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) at 25°C require nucleophilic attack at the corner protonated species

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*Footnote: The acetate mixture was subsequently reduced with $LiAlH_4$.

(75) to account for only 3 % of the reaction pathway, collapse of this species to the tertiary carbocation (76) and subsequent proton elimination or nucleophilic attack accounting for the remaining 97 % of the reaction pathway (Appendix B). The higher ratio of nucleophilic capture to elimination in the addition of methanol to (76); (78:22) as compared to the acetolysis of 2-(4-methylcyclohex-3-enyl)ethyl brosylate[100] (18:55) is a reflection of the better nucleophilicity of methanol as compared with acetic acid.

In the reaction of (35) with mercuric acetate, the 9:1 ratio of (72c):(73c) requires nucleophilic capture of the corner mercurated species (75c) to the extent of ca. 82 %. This reflects the lesser charge development at C2 in the oxymercuration reaction, a consequence of the greater orbital interaction between C2 and C4 (Chapter 2) in (75c).

The reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane with methanol-d_1, p-toluenesulphonic acid at 80°C for 7 days yielded deuterated 2-methylbicyclo[3.2.1]oct-2-ene, 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane, 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane and

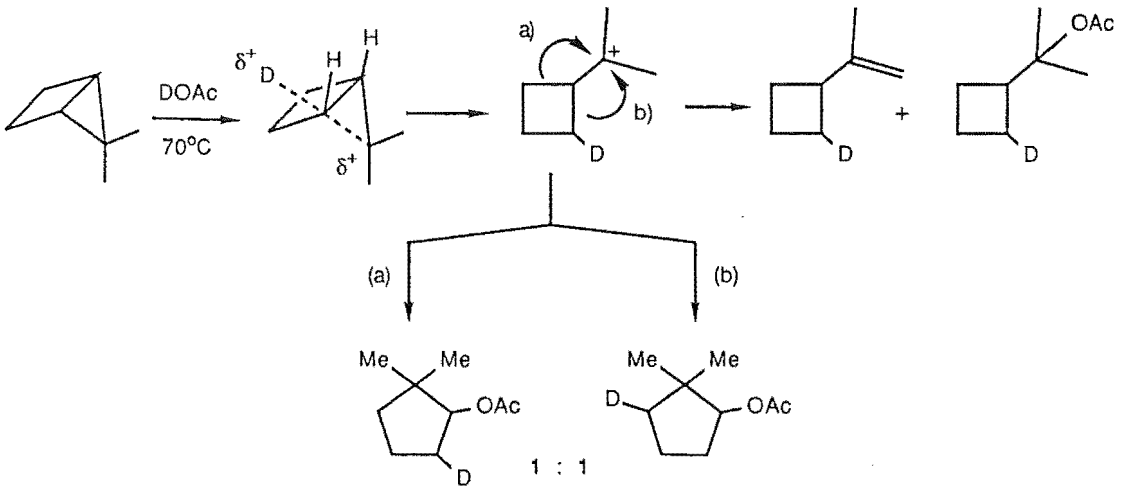
Compound	Excess Deuterium (atom %)			
	D4endo	D3exo	D3endo	Methyl
(74)	98	82		246
(72)	243			220
(73)	227			257

Table 11

Excess deuterium from the acid catalysed addition of methanol - d_1 to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane at 80°C.

2-methoxy-1-methylbicyclo[2.2.2]octane in a similar ratio to that previously obtained. The deuterium distribution, obtained

from mass spectrometry and ^{2}H and ^{13}C nmr, and shown in Table 11, is consistent with the multiple addition / elimination mechanism shown in Scheme 34. The observation of a deuterium at C5a and not C5s of deutero (81) requires nucleophilic attack at the bridged cation (80) to occur before relaxation to the free carbocation is possible. The deuterium incorporation at C3 and the methyl in each of the compounds arises from repeated methanol addition to 2-methylbicyclo[3.2.1]oct-2-ene (74), 2-methylenebicyclo[3.2.1]octane (79) and elimination at the epimeric ethers (72) and (73). The C4-endo deuterium arises from initial deuteron attack with inversion at the cyclopropyl ring.



Scheme 36

Free carbocation formation in the acetic acid-d_1 addition to 5,5-dimethylbicyclo[2.1.0]pentane.

The requirement for a free tertiary carbocation in the acid catalysed methanol addition to 2-methyl-endo-tricyclo-[3.2.1.$0^{2,4}$]octane (35), while being unusual for proton attack on cyclopropanes, is not unique. The acetolysis of 5,5-dimethylbicyclo[2.1.0]pentane has been found to proceed via a tertiary carbocation[103] (Scheme 36), as evidenced by the scrambling of deuterium between the C3 and C5 positions in the

isolated 1-acetoxy-2,2-dimethylcyclopentane. Here, the ability to form the most stable carbocation takes precedence over all other factors. In contrast, the acetolysis of bicyclo[2.1.0]pentane is thought to proceed via. a corner protonated cyclopropane, the free cyclopentyl cation playing a negligible role in the reaction pathway.[103]

Appendix B

For 100 molecules, nucleophilic attack at (75a) will account for $100A_{(72)}$ of (72a), nucleophilic attack or proton loss at (76a) accounting for the remainder (Path B). Hence,

$$100 = A_{(72)} + B_{(72)} + B_{(73)} + B_{(74)}$$

$B_{(x)}$ being the percent of product 'x' formed via path B, $A_{(72)}$ being the percent of (72) formed from cation (75). Since $B_{(74)} = 22$, $B_{(73)} = 41$, and $B_{(72)} = 33.5$ (since $B_{(72)}$ is assumed to be 45/55 $B_{(73)}$) we have

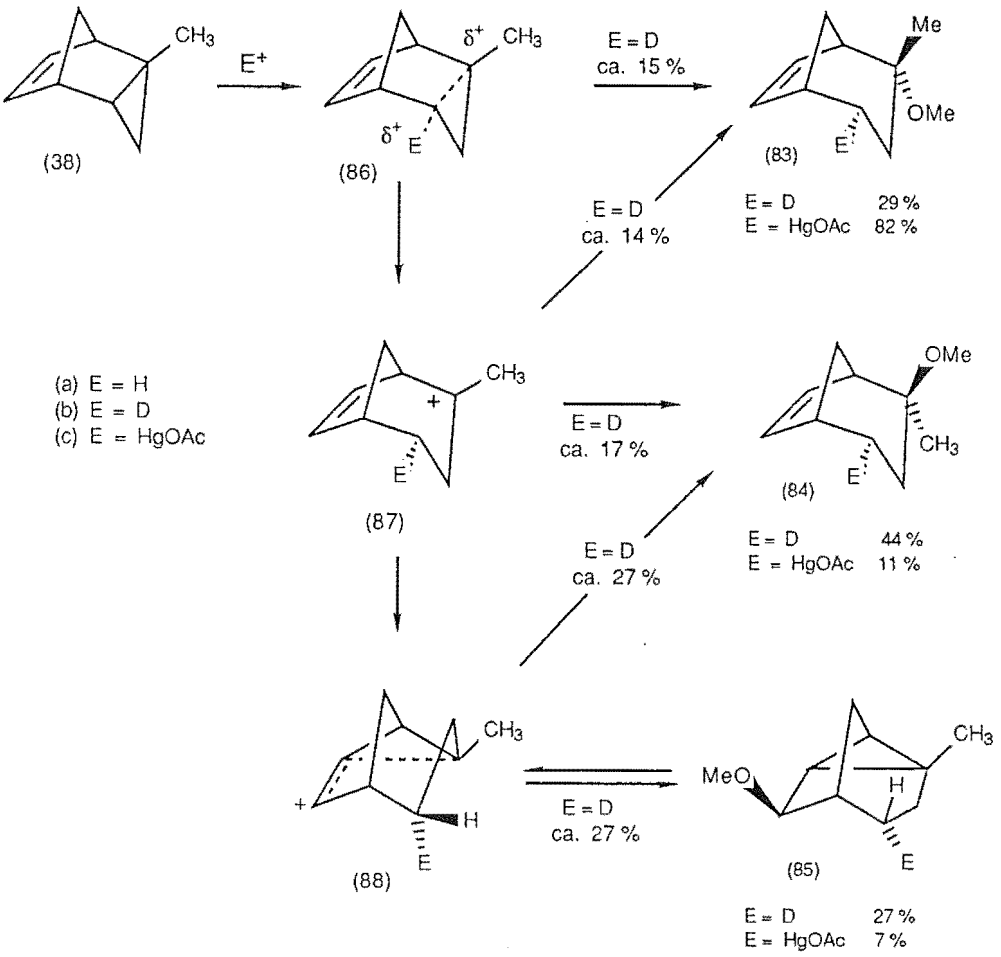
$$100 = A_{(72)} + 96.5,$$

$$\text{or } A_{(72)} = 3.5$$

That is, nucleophilic attack at (75) accounts for 3 % of the reaction pathway, reaction at the free cation (76) comprising the remainder (97 %). A similar analysis for mercuric acetate attack requires nucleophilic attack at (75c) to the extent of 82 %.

C) Protonation and mercuration of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene

The acid catalysed reaction of 2-methyl-endo-tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene (38) with methanol at room temperature for 3 days (87 % reaction) gave 3 compounds (Scheme 37), subsequently shown to be 2-exo-methoxy-2-endo-methyl-



Scheme 37

Room temperature reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with (a) H^+ (D^+) (b) $Hg(OAc)_2$

bicyclo[3.2.1]oct-6-ene (84a), 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83a) and 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85a) in the ratio of 38:29:33 respectively. Separation was achieved on a silver nitrate

(10 %) impregnated silica column.

The identity of 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]-oct-6-ene (84a) was determined by hydrogenation to 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a), identical with authentic sample (Chapter 4b). The ^{1}H nmr of (84a) was assigned by comparison with that of 2-endo-methyl-bicyclo[3.2.1]oct-6-en-2-exo-ol[92a], and by selective decoupling and difference NOE's. In particular, the exo stereochemistry of the methoxy methyl follows from a difference NOE spectrum. Irradiation at H8s (1.95 ppm), so assigned due to a coupling with H8a (1.72 ppm, 10.0 Hz) and a lack of coupling with H1 / H5 gives enhancements at the methoxy methyl (3.19 ppm, 0.8 %), H1 / H5 (2.54 ppm, 1.0 %), H8a (1.72 ppm, 12.5 %), H4-exo (1.62 ppm, 2.5 %) and the methyl (1.03 ppm, 0.4 %). A heteronuclear correlation experiment identified connectivities between, amongst others, H4-exo 1.62 ppm and H4-endo 1.23 ppm / C4, 22.2 ppm and H8s 1.95 ppm and H8a 1.72 ppm / C8, 38.8 ppm. A coupling between the C4-H at 1.23 ppm and H8a of 2.3 Hz confirms the assignment of this proton as C4-endo-H.

The identity of 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]-oct-6-ene (83a) was similarly determined. The ^{13}C nmr was assigned from the expected effect of addition of a double bond to 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a). A heteronuclear correlation spectrum subsequently allowed assignment of the carbon, proton connectivities, in particular those of H4-exo and H4-endo, 1.42 ppm - 1.34 ppm / C4, 23.0 ppm and H8s 1.49 ppm and H8a 1.87 ppm / C8, 40.7 ppm. While the chemical shifts of H4-exo and H4-endo were not able to be resolved, the presence of coupling from H4-endo to H8a (1.87

ppm, 1.7 Hz) and H3-endo (1.65 ppm, 3.6 Hz) and from H4-exo to H3-endo (11.6 Hz) allows identification of the stereochemistry of deuteron at C4.*

The identity of 6-exo-methoxy-2-methyltricyclo-[3.2.1.$0^{2,7}$]octane (85a) follows from comparison with the reported ^{1}H nmr spectra of 2-methyltricyclo[3.2.1.$0^{2,7}$]octan-6-exo-ol[92a] and the previously obtained 6-exo-methoxytricyclo-[3.2.1.$0^{2,7}$]octane (71a; Chapter 3c). A Eu(fod)$_3$ study was performed (Fig. 25), the results supporting the assignment of (85a). Comparison with the ^{1}H nmr of 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane reveals a loss of coupling of ca. 7 Hz from the cyclopropyl proton at 1.30 ppm, indicating the methyl is substituted at the cyclopropyl ring. Upon irradiation of the methyl at 0.92 ppm, a difference NOE spectrum showed enhancements at H3-exo/H3-endo (1.66 - 1.60 ppm, 2.2 % total), H7 (1.30 ppm, 6.4 %) and H1 (1.19 ppm, 5.0 %), thereby confirming the presence of a methyl at C2. The methoxy group was established as C6-exo from comparison with the couplings at the C6-H observed for 2-methyltricyclo-

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*Footnote: (83a) obtained from the addition of methanol to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene at 25°C was identical with the major product from sodium mercury amalgam reduction in NaOH of 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene, the major product from the reaction of mercuric acetate / methanol with hydrocarbon (38). Hydrogenation of the so produced (83a) gave 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a), identical with authentic sample (Chapter 4b). The coupling between H3-exo (1.48 ppm) and H4-exo and H4-endo in undeuterated (83a) was unable to be determined.

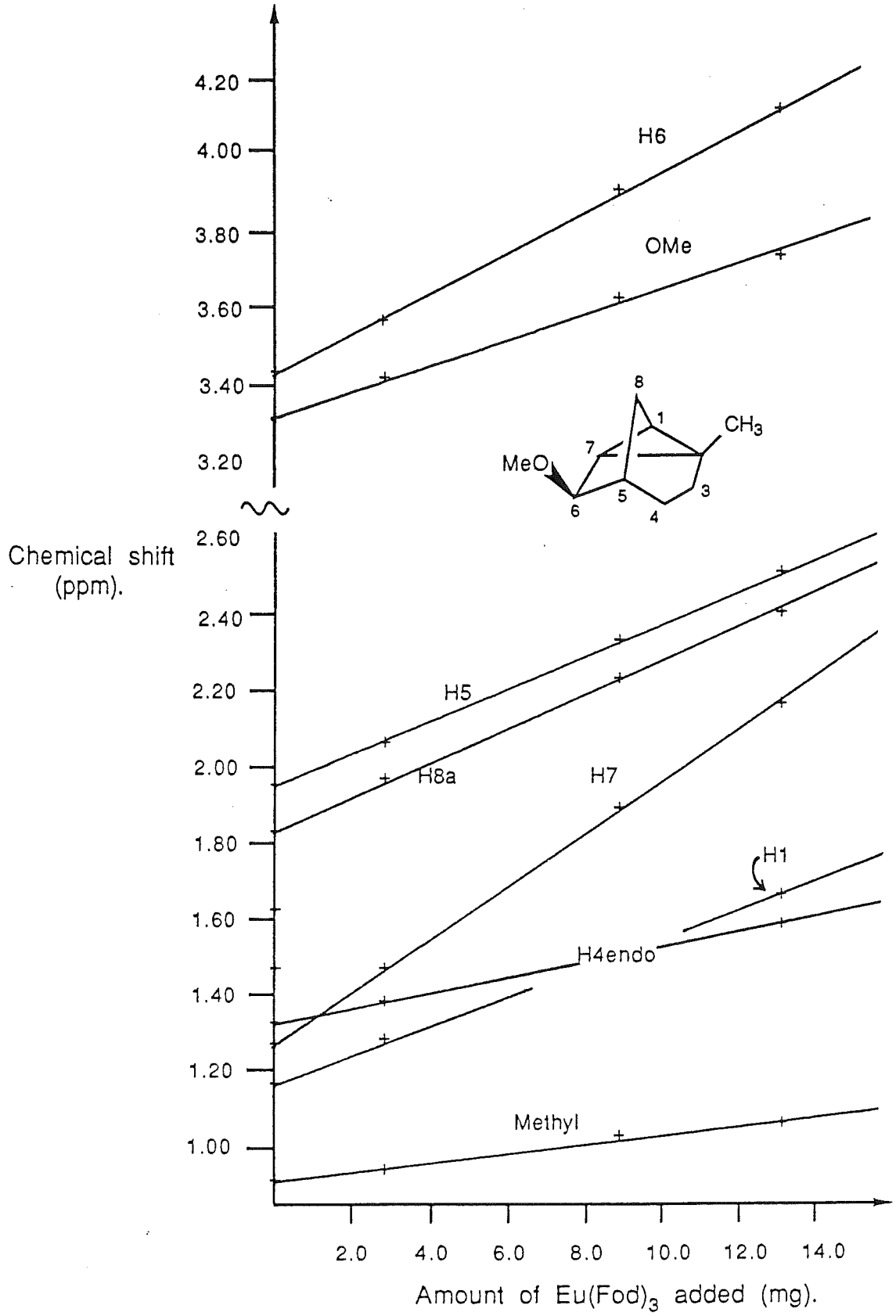

Figure 25

$Eu(Fod)_3$ shifts induced in the ^1H nmr of 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane.

[3.2.1.$0^{2,7}$]octan-6-exo-ol[92a]. H6-endo for both these compounds appears in the ^{1}H nmr as a singlet.* Irradiation at H6-endo (3.44 ppm) in a difference NOE experiment gave enhancements at the methoxy methyl (3.33 ppm, 4.3 %), H5 (1.98 ppm, 1.8 %), H4-endo (1.37 ppm, 2.1 %) and H7 (1.30 ppm, 2.1 %), confirming the methoxy stereochemistry and allowing assignment of H4-endo at 1.37 ppm. Coupling between H4-endo and H8a at 1.82 ppm (2.1 Hz) further confirms assignment of H4-endo. A heteronuclear correlation spectrum identified H4-exo at 1.51 ppm.

The stability of the primary reaction products under the reaction conditions was determined by separately stirring each in methanol with p-toluenesulphonic acid at room temperature for 21 days. 2-endo-Methoxy-2-exo-methylbicyclo[3.2.1]-oct-6-ene (83a) was stable under these conditions. However, 2-exo-methoxy-2-endo-methylbicyclo[3.2.1oct-6-ene (84a) gave 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85a) along with (84a) in the ratio of 1:9. 6-exo-Methoxy-2-methyl-tricyclo[3.2.1.$0^{2,7}$]octane (85a) proved even less stable, giving a 1:1 mixture of 2-exo-methoxy-2-endo-methylbicyclo-[3.2.1]oct-6-ene (84a) and (85a) after 22 hours. This product ratio was invariant for 21 days. Such a rearrangment is in direct contrast to the reaction of 6-exo-methoxytricyclo-[3.2.1.$0^{2,7}$]octane (71a) to give bicyclo[2.2.2]oct-5-ene (70a) along with (71a) upon reaction with p-toluenesulphonic acid in methanol for 2 hours. Reaction of the p-toluenesulphonate of 2-methyltricyclo[3.2.1.$0^{2,7}$]octane-6-exo-ol with

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*Footnote: For 2-methyltricyclo[3.2.1.$0^{2,7}$]octan-6-endo-ol, H6-exo appears as a quartet with couplings of 4.5 Hz and 4.0 Hz to H5 and H7 respectively.[92a]

p-toluenesulphonylchloride in pyridine has similarly been found to yield 2-endo-methylbicyclo[3.2.1]oct-6-en-2-exo-ol (11 %), in addition to 2-methylbicyclo[3.2.1]octa-2,6-diene (50 %) and 2-methylenebicyclo[3.2.1]oct-6-ene (3 %).[92a] The solvolysis of (85b), giving a mixture of (84b) and (85b), is consistent with the intermediacy of cation (88b), nucleophilic attack on this species giving (84b) and (85b) in the ratio of 1:1. The absence of (83) from solvolysis of (85b) indicates nucleophilic attack on the classical tertiary cation (87), if it is indeed present, is uncompetitive with attack on (88).

Nucleophilic attack at the intially formed protonated cyclpropane (86a) is competitive with collapse to the free tertiary cation (87a), in a manner similar to that observed in the protonation of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35). However, the tertiary cation (87a) is sufficiently stable and long lived to allow conformational change to allow interaction between the positive charge at C2 and the pi system, resulting in the formation of (88a). This interconversion is similar to that observed in the reaction of hydrocarbon (38) with tetracyanoethene[78] (Scheme 31). Unlike the reaction with tetracyanoethene, nucleophilic attack at (87a) is competitive with rearrangement. Given the instability of (85a) to the reaction conditions, the degree of involvement of the two cations (87) and (88) cannot be stated with any certainty, since 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]-oct-6-ene may arise from either initial methanol addition to hydrocarbon (38) or from subsequent decomposition of 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$octane. However if we assume 27 % of (84b) arises from subsequent decomposition of (85b) then, under kinetic control, approximately 54 % of the reaction pathway will proceed through cation (88b). Therefore,

nucleophilic attack at the protonated cyclopropane (86b) occurs to the extent of 15 %, nucleophilic attack at (87b)* accounting for the remaining 31 %. This requires a greater degree of nucleophilic attack (approximately 15:3) at the protonated cyclopropane (86a) than is the situation with 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35). Such a result is not inconsistent with a -I effect by the double bond, initially disfavouring the presence of any positive charge at C2.

The reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with mercuric acetate in methanol, and subsequent sodium mercury amalgam reduction in sodium hydroxide, gave 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (82 %), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (11 %) and 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (7 %), identical with those previously obtained from the acid catalysed methanol addition at 25°C. Hydrogenation of the crude reduction mixture gave a mixture containing mainly 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a), identical with authentic sample (Chapter 4b). While the original organomercurial mixture was not able to be separated, the 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]oct-6-ene (83c) was present in sufficient yield to allow determination of its spectroscopic data. The ^{13}C-^{199}Hg couplings are consistent with a 4-endo-acetoxymercurio group

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*Footnote: This calculation assumes the ratio of exo to endo attack at cation (87b) by methanol to be similar to the 55:45 ratio observed for nucleophilic attack at the analogous cation (76) (Chapter 4b).

(Chapter 2); (J ^{13}C-^{199}Hg: C1, 25 Hz; C2, not obs.; C3, 64 Hz; C4, 1641 Hz; C5, 74 Hz; C6, 34 Hz; C7, not obs.; C8, 299 Hz.). A heteronuclear correlation spectrum subsequently allowed assignment of the carbon - proton connectivities and, in conjunction with selective decoupling, assignment of the ^{1}H nmr. A difference NOE spectrum of the crude organomercurial mixture, with irradiation of H8s at 1.55 ppm, gave enhancements at H4-exo/H5 (ca. 2.9 ppm, 11.6 % total), H1 (2.56 ppm, 2.7 %), H8a (1.97 ppm, ca. 13 %) and the methyl (1.29 ppm, 1.8 %), further confirming the exo stereochemistry of C4-H (and the methyl). To confirm the stereochemistry of the acetoxymercurio group, a sodium mercury amalgam reduction of the crude organomercurial mixture in sodium deuteroxide was carried out. This gave 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]oct-6-ene (83b), 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84b) and 4-deutero-6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85b). The major component (83b) was separated by preparative glc. The presence of a C4-endo-deuterium in (83b) after the stereospecific reduction was confirmed by the presence of a triplet in the ^{13}C nmr at 22.6 ppm and the loss of a coupling from H4-endo to H8a (1.7 Hz) and H3-endo (3.6 Hz). The magnitude of the coupling from H3-endo to H4-exo (12.5 Hz) and also from H3-exo to H4-exo (5.3 Hz) further supports the assignment of the deuterium stereochemistry. The deuterium sterochemistry in 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84b) was similarly established as C4-endo due to the presence of a triplet in the ^{13}C nmr at 21.7 ppm and a peak in the ^{2}H nmr at 1.20 ppm corresponding to C4-endo-deuterium. While the deuterium sterochemistry in (85b) was not determined, it would be expected that, by comparison with (83b) and (84b)

the deuterium be at C4-endo. Given the stereospecific nature of the organomercurial reduction, it is therefore apparent that the mercuric salt attacks the cyclopropane ring with inversion of configuration to give (83c) and (84c), and by implication, (85c). The higher degree of unrearranged product (83c) as compared to the reaction with proton (deuteron) is indicative of the lack of substantial charge development in the reaction with mercuric acetate (Chapters 2 and 3).

To determine the stereochemistry of proton attack on the cyclopropane ring, the acid catalysed addition of methanol-d_1 to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene was examined at room temperature. Reaction for 7 days (79 % reaction) gave 4-endo-deutero-2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]oct-6-ene (83b), 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84b) and 4-endo-deutero-6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85b) in the ratio of 29:44:27 respectively. The 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83b) was identical in all respects to (83b) obtained from sodium mercury amalgam reduction in sodium deuteroxide of the organomercurial mixture from the reaction of hydrocarbon (38) with mercuric acetate in methanol. For product (84b), the presence of a triplet in the ^{13}C nmr at 21.7 ppm and a peak at 1.22 ppm in the ^{2}H nmr, along with a loss of a coupling from H8a (1.72 ppm) to H4-endo (2.3 Hz), is consistent with a C4-endo-D. For (85b) the presence of a C4-endo deuterium similarly follows from the presence of a triplet in the ^{13}C nmr at 25.4 ppm and a peak in the ^{2}H nmr at 1.32 ppm in addition to a loss of coupling from H8a (1.82 ppm) to H4-endo of 2.1 Hz.

In all of the products from the acid catalysed methanol-d_1 addition to (38), the deuterium is at C4-endo,

consistent with initial corner attack by the deuteron. Similarly to the analogous endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37), the HOMO of hydrocarbon (38) would be expected to contain a contribution from the Walsh e_s orbital*, the C6,C7 pi bond, and the C1,C8 / C5,C8 sigma orbitals, in addition to a contribution from the methyl group. Electrophilic attack at the edge of the C2,C4 cyclopropyl bond of hydrocarbon (38) is unfavourable due to a secondary orbital interaction between the electrophile LUMO and the C1,C8 / C5,C8 contribution to the hydrocarbon HOMO (Chapter 2). There are no significant unfavourable interactions for protonation (mercuration) at the corner of C4, and therefore attack at this position is observed. The observation of exclusive protonation at the cyclopropyl ring and not the double bond reflects the kinetic favourability of this process (Chapter 2), further enhanced by the presence of a methyl group at C2. Mercuration similarly occurs at the cyclopropyl ring as a consequence of the greater charge stabilisation possible with the C2 methyl.

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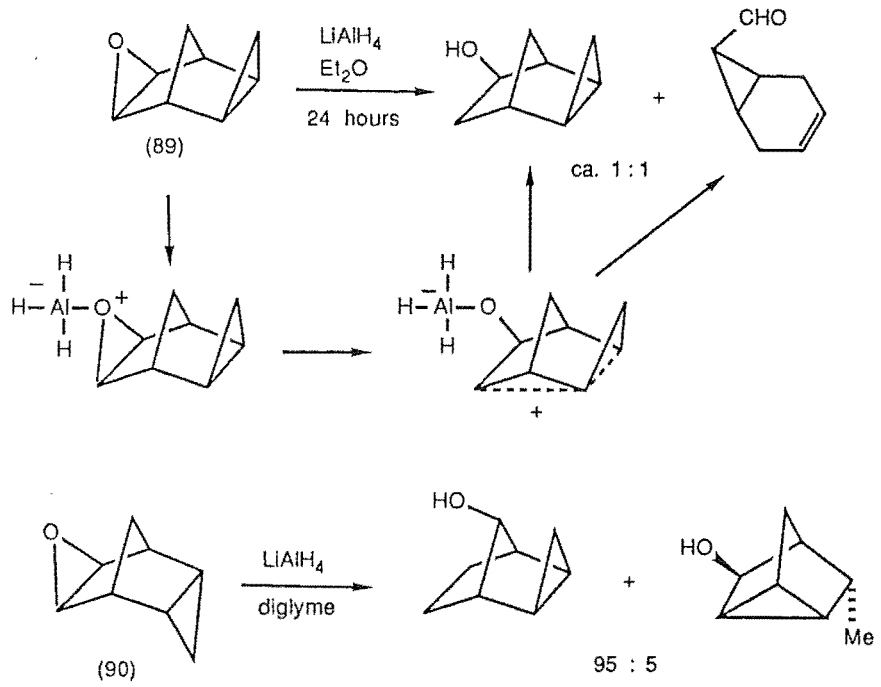
*Footnote: In the absence of any experimental or theoretical data for 1,1,2-trisubstituted cyclopropanes, it must be assumed that, by analogy with endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37), the Walsh e_s orbital is destabilised relative to the Walsh e_a orbital.

Chapter 5

A) Introduction

Bromine addition to a double bond is faster than the corresponding addition to a cyclopropane ring, the latter being slow in the absence of Lewis acid catalysts (Chapter 1). Hence, it would be expected that the bromination of exo- and endo- tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) and (37) would occur by initial attack at the pi system. The different relative geometries of the cyclopropyl ring to the double bond will result in the cation produced by electrophilic attack giving different products of reaction. This is shown in the lithium aluminium hydride reduction of 6-exo-epoxy- exo- and endo-tricyclo[3.2.1.$0^{2,4}$]octane (89) and (90), where the exo isomer (89) undergoes reduction to give both unrearranged and rearranged products[104] while reduction of endo (90) gives only rearranged products[105] (Scheme 38).

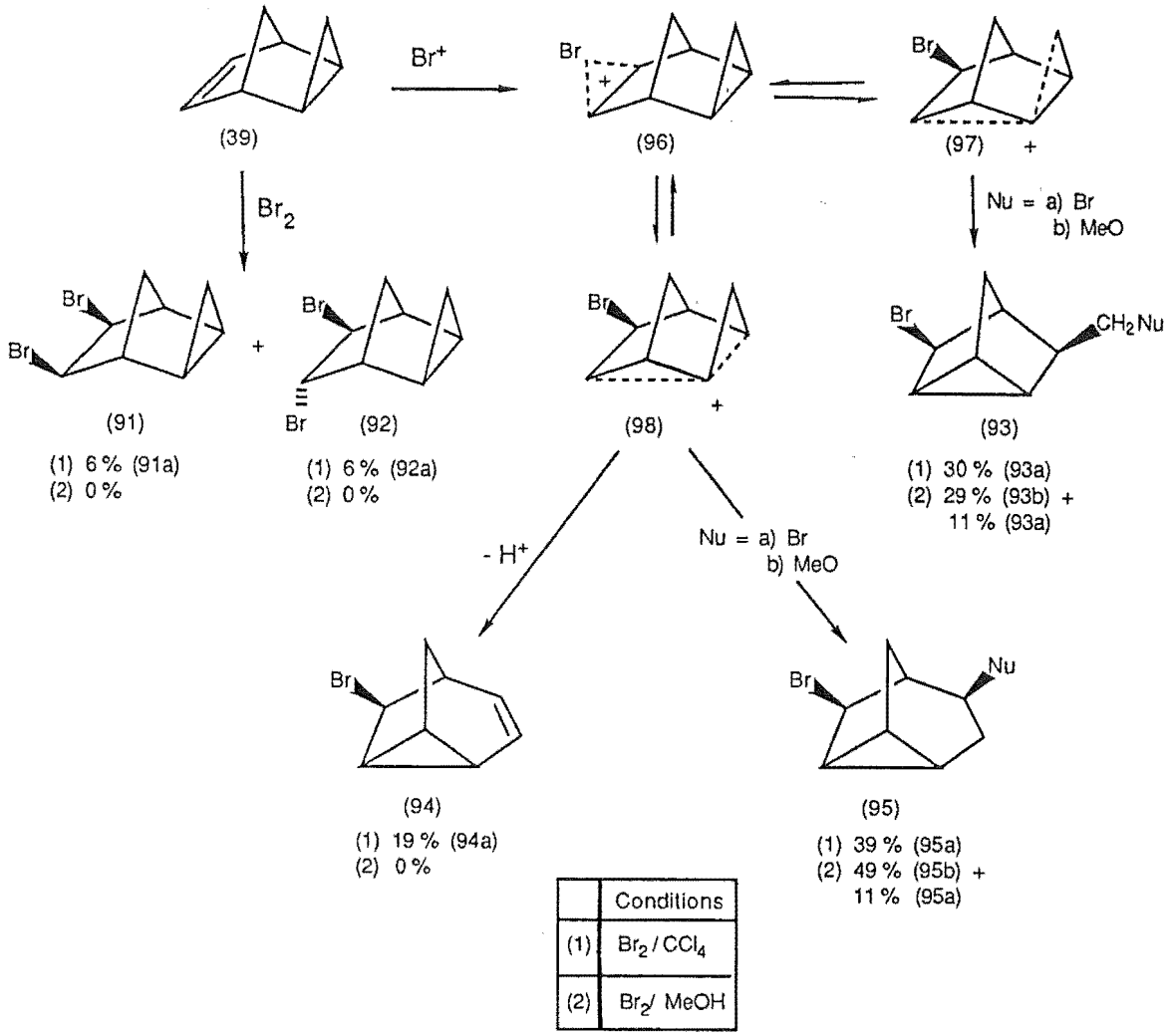


Scheme 38

$LiAlH_4$ reduction of the epoxides (89) and (90) from exo- and endo- tricyclo[3.2.1.$0^{2,4}$]oct-6-ene.

B) Bromination of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene

The reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with a 0.88 molar equivalent of bromine in carbon tetrachloride was instantaneous at room temperature. Glc identified five major products (Scheme 39), subsequently shown to be



Scheme 39

Reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with Br_2 in 1) CCl_4 2) MeOH

6-exo-7-exo-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (91a; 6 %), 6-endo-7-exo-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (92a; 6 %), 5-exo-bromo-3-exo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (93a; 30 %), 6-exo-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene (94a; 19 %) and

4-exo-6-exo-dibromotricyclo[3.2.1.$0^{2,7}$]octane (95a; 39 %). Separation was achieved by radial chromatography on silica.

6-exo-Bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene (94a) was identified by comparison of the observed ^{1}H nmr spectrum with that previously reported.[106]

The identity of 6-endo-7-exo-dibromo-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (92a) was determined as follows. A heteronuclear correlation spectrum identified the two CHBr groups H6-exo, 4.38 ppm / C6, 63.0 ppm and H7-endo, 3.93 ppm / C7, 59.5 ppm, the chemical shifts (^{1}H and ^{13}C) being consistent with the presence of a bromine substituent. The trans stereochemistry of the C6-H and C7-H was established from the presence of a small coupling between H7-endo and H6-exo (3.2 Hz). A coupling between C7-endo-H and C8-syn-H at 1.12 ppm (3.2 Hz) shows that the C7-H is endo. This is similar to that observed for the analogous 6-endo-7-exo-dibromo-3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]octane[107], the two CHBr peaks appearing as triplets (J = 3 Hz) at 4.37 ppm and 3.95 ppm. The presence of an exo cyclopropyl group in (92a) follows by comparison of the chemical shifts (^{1}H and ^{13}C), and the magnitude of the coupling, with those of exo-tricyclo[3.2.1.$0^{2,4}$]octane (36). For the trans dibromide (92a), a heteronuclear correlation spectrum shows connectivity between H3-exo at 0.67 ppm, and H3-endo at 0.32 ppm, with C3 at 4.2 ppm.* Similarly, for exo-tricyclo[3.2.1.$0^{2,4}$]octane (36), H3-exo at 0.28 ppm and H3-endo at -0.11 ppm exhibit connectivity with C3

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*Footnote: The relevant proton-proton couplings for (92a) are as follows: $^{2}J_{3exo,3endo}$ 6.3 Hz, $^{3}J_{3exo,2} = {}^{3}J_{3exo,4}$ 3.2 Hz, $^{3}J_{3endo,2} = {}^{3}J_{3endo,4}$ 7.1 Hz.

at 1.0 ppm, with coupling between H3-exo and H3-endo (6.0 Hz), H3-exo and H2 (3.1 Hz), H3-exo and H4 (3.1 Hz), H3-endo and H2 (7.0 Hz) and H3-endo and H4 (7.0 Hz). Further support for the cyclopropyl stereochemistry can be found in a difference NOE spectrum, irradiation of (92a) at H8s (1.12 ppm), so assigned due to the presence of coupling with H8a (1.42 ppm, 11.8 Hz) and H7-endo (3.93 ppm, 3.2 Hz), giving enhancements at H1/5 (2.55 ppm, 1.0 %), H8a (1.42 ppm, 7.4 %) and H3-exo (0.67 ppm, 7.3 %).

For 6-exo-7-exo-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]-octane (91a), the ^{1}H nmr and ^{13}C nmr require the product to contain a plane of symmetry. The presence of a CHBr group at 4.21 ppm (C6,7 56.7 ppm) with coupling to H8s (1.06 ppm, 2.3 Hz) requires C6-H (C7-H) to be endo. This is similar to that observed for 6-exo-7-exo-dibromo-3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]octane[107], H6-endo (H7-endo) appearing as a doublet (J 2 Hz) at 4.10 ppm. The presence of an exo cyclopropyl group in (91a) follows from the chemical shifts (H3-exo 0.72 ppm, H3-endo 0.38 ppm, C3 6.1 ppm) and the coupling ($^{2}J_{3endo,3exo}$ 6.3 Hz, $^{3}J_{3endo,2} = {}^{3}J_{3endo,4}$ 7.0 Hz, $^{3}J_{3exo,2} = {}^{3}J_{3exo,4}$ 3.0 Hz), these values being comparable with those previously quoted for exo-tricyclo[3.2.1.$0^{2,4}$]-octane.

A heteronuclear correlation spectrum of 4-exo-6-exo-dibromotricyclo[3.2.1.$0^{2,7}$]octane (95a) identified the CHBr groups H4-endo, 4.14 ppm / C4, 47.8 ppm and H6-endo, 4.30 ppm / C6, 55.2 ppm. The presence of H6 (4.30 ppm) as a singlet, $W_{h/2}$ 3 Hz, identifies the stereochemistry of the C6-H as endo, similar to that observed for 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85a; Chapter 4c). The magnitude of the coupling from C4-H at 4.14 ppm to

H3-endo (2.52 ppm, 7.0 Hz), H3-exo (2.39 ppm, 7.0 Hz), H8a (2.20 ppm, 1.5 Hz), along with a further coupling to H5 (2.55 ppm, 1.5 Hz) compares with those observed in the analogue 2-methyltricyclo[3.2.1.$0^{2,7}$]octan-6-exo-ol.[92a] * The stereochemistry of the C4-H was determined from difference NOE spectra. Irradiation at H4 (4.14 ppm) gave enhancements at H6-endo (4.30 ppm, 4.0 %), H5/H3-endo (ca. 2.54 ppm, 5.0 % total) and H3-exo (2.39 ppm, 0.6 %). In addition, irradiation at H3-endo and H5 at 2.54 ppm gave enhancements at H6-endo (4.30 ppm, 1.0 %), H4-endo (4.14 ppm, 4.3 %), H3-exo (2.39 ppm, 8.1 %) and H2 (1.00 ppm, 1.0 %). The large enhancement from H4 to H6-endo (4.0 %) allows assignment of the C4-endo-H at 4.14 ppm. Evidence for the presence of an endocyclic cyclopropyl group is found in the coupling between the cyclopropyl protons, in particular the couplings of C2-H ($^3J_{2,1} = {}^3J_{2,7}$ 7.0 Hz, $^3J_{2,3endo}$ 3.4 Hz, $^3J_{2,3exo}$ 1.9 Hz) and H7 ($^3J_{7,1} = {}^3J_{7,2}$ 6.6 Hz, $^4J_{7,5} = {}^4J_{7,8s}$ 1.3 Hz). The connectivity observed between H1, 1.67 ppm / C1, 18.0 ppm; H2, 1.00 ppm / C2, 18.4 ppm and H7, 1.85 ppm / C7, 25.3 ppm, and in particular, the appearance of C1, C2 and C7 as methine carbons in an APT spectrum is consistent with the structure of (95a).

For 5-exo-bromo-3-exo-bromomethyltricyclo[2.2.1.$0^{2,6}$]-heptane (93a), a heteronuclear correlation spectrum identified connectivities between H5, 3.96 ppm / C5, 55.9 ppm and H8a, 3.28 ppm and H8b, 3.18 ppm / C8, 32.4 ppm. The exo stereochemistry of the $C8H_2$ was determined from a difference NOE spectrum, irradiation at H8a and H8b (3.30 ppm -

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*Footnote: $^3J_{3exo,4exo} = {}^3J_{3endo,4endo}$ 11.0 Hz, $^3J_{3endo,4exo} = {}^3J_{3exo,4endo}$ 4.5 Hz.

3.15 ppm) giving enhancements at H4 (2.22 ppm, 1.6 %), H3 (2.12 ppm, 2.6 %), H7s (1.52 ppm, 5.1 %) and H2 (1.30 ppm, 1.6 %). The stereochemistry of the C5-H similarly followed from a difference NOE spectrum, irradiation at H5-endo (3.96 ppm) giving enhancements at H4 (1.4 %), H3 (4.7 %) and H6 (1.67 ppm, 1.3 %), but not the CH_2Br at 3.28 ppm and 3.18 ppm. The couplings between the cyclopropyl protons ($^3J_{1,2} = {}^3J_{1,6}$ 5.2 Hz, $^3J_{2,6}$ 5.2 Hz), along with the multiplicity of C1, C2 and C6 as determined by an APT spectrum, requires the presence of an endocyclic cyclopropyl group.

To determine the position of initial attack by electrophilic bromine, the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with bromine in methanol was examined. This gave four products in 84 % isolated yield, subsequently shown to be 5-exo-bromo-3-exo-bromomethyltricyclo-[2.2.1.$0^{2,6}$]heptane (93a; 11 %), 4-exo-6-exo-dibromotricyclo-[3.2.1.$0^{2,7}$]octane (95a; 11 %), 5-exo-bromo-3-exo-methoxy-methyltricyclo[2.2.1.$0^{2,6}$]heptane (93b; 29 %) and 6-exo-bromo-4-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (95b; 49 %). Separation was achieved by radial chromatography. The regiochemistry of the methoxy group, introduced by nucleophilic attack at an intermediate carbocation, was determined by examination of the chemical shift differences in the ^1H and ^{13}C nmr spectra upon substitution of a bromine with a methoxy. The magnitude of such a shift will be dependent upon the proximity of the proton (carbon) nucleus to the methoxy group. For both 6-exo-bromo-4-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (95b) and 5-exo-bromo-3-exo-methoxymethyltricyclo[2.2.1.$0^{2,6}$]heptane (93b), the coupling constants for each of the protons in the ^1H nmr are of the same magnitude as those observed with the corresponding dibromides, consistent with the same carbon

skeleton and stereochemistry as previously observed for (93a) and (95a).

For 6-exo-bromo-4-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (95b), the changes in chemical shift upon substitution with a methoxy (Table 12) are consistent with the presence of a methoxy group at C4.* Evidence for the endo stereochemistry at the C4-H was found in a difference NOE spectrum, irradiation of H6-endo at 4.22 ppm giving enhancement at H4-endo (3.27 ppm, 3.2 %), H5 (2.44 ppm, 1.6 %), H3-endo (2.15 ppm, 0.8 %) and H7, (1.77 ppm, 1.6 %) but not the methoxy methyl at 3.23 ppm.

For 5-exo-bromo-3-exo-methoxymethyltricyclo[2.2.1.$0^{2,6}$]-heptane (93b) the changes in carbon and proton chemical shifts (Table 13)* are consistent with the presence of a methoxy group at C8. That C5-H in (93b) is endo follows from the appearance of a singlet in the ^{1}H nmr at 3.95 ppm.

The presence of 6-exo-bromo-4-exo-methoxytricyclo-[3.2.1.$0^{2,7}$]octane (95b) and 5-exo-bromo-3-exo-methoxytricyclo-[2.2.1.$0^{2,6}$]heptane (93b) is consistent with initial attack by Br^{+} at the double bond with subsequent rearrangement and nucleophilic attack (Scheme 39). Rearrangement of the initially formed (96) can occur with participation of the C2,C3 cyclopropyl bond to give (93), or with participation of the internal C2,C4 cyclopropyl bond to give (94) and (95). Such a mechanism has been proposed to explain the results from the acetolysis of the bromobenzenesulphonates of exo-tricyclo[3.2.1.$0^{2,4}$]octan- 6-exo- and 6-endo- ol.[108] A similar propensity towards rearrangement is found in the electrophilic addition of bromine to the structurally similar

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*Footnote: A heteronuclear correlation spectrum identified all of the carbon-proton connectivities.

Compound	Nucleus	1	2	3exo	3endo	4endo	5	6endo	7	8s, 8s
(95a)	^{1}H	1.67	1.00	2.39	2.52	4.14	2.55	4.30	1.85	2.20
	^{13}C	18.0	18.4	29.6		47.8	49.8	55.2	25.3	23.0
(95b)	^{1}H	1.60	0.95	1.67	2.15	3.27	2.44	4.22	1.77	1.95
	^{13}C	18.1	16.1	25.0		77.5	44.5	56.3	25.7	21.0

Table 12

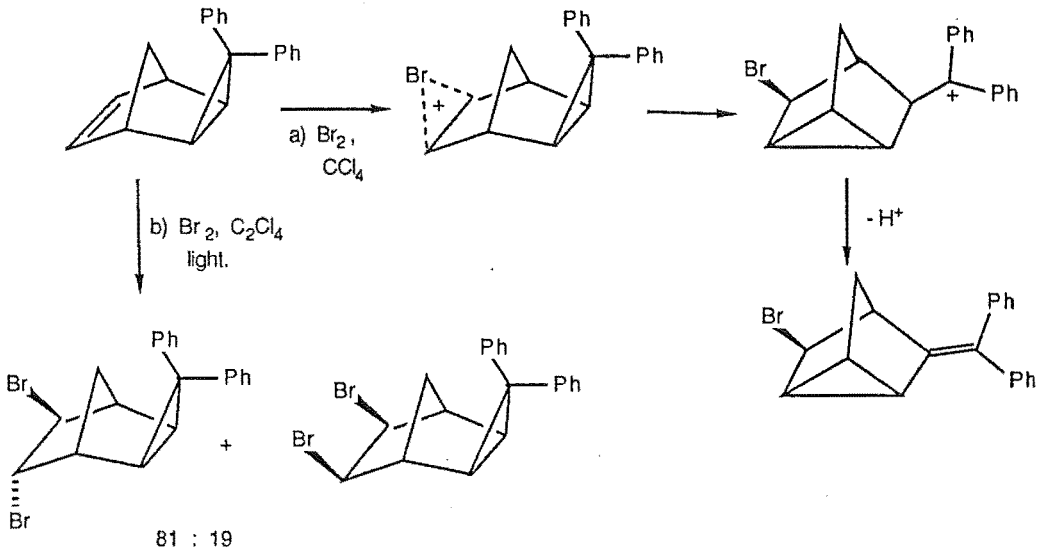
Comparison of the nmr data (^{1}H and ^{13}C) for dibromo- (95a) and bromo-methoxy- (95b).

Compound	Nucleus	1	2	3	4	5	6	7a	7s	8a	8b
(93a)	^{1}H	1.44	1.30	2.12	2.22	3.96	1.67	2.05	1.52	3.28	3.18
	^{13}C	11.7	18.8	46.1	40.9	55.9	20.8	27.0		32.4	
(93b)	^{1}H	1.38	1.19	1.92	2.13	3.95	1.55	1.95	1.53	3.26	3.21
	^{13}C	11.7	16.7	43.3	39.2	57.0	19.6	27.3		72.4	

Table 13

Comparison of the nmr data (^{1}H and ^{13}C) for dibromo- (93a) and bromo-methoxy- (93b).

3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[107] (Scheme 40a), the product of this reaction being 5-exo-bromo-3-methylene-8,8-diphenyltricyclo[2.2.1.$0^{2,6}$]heptane.



Scheme 40

The reaction of 3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with a) Br^+ b) $Br^\bullet$

In the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) with bromine in carbon tetrachloride, 6-exo-7-exo-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (91a) and 6-endo-7-exo-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (92a) probably arise from bromine radical attack at the double bond. Electrophilic Br_2 addition to yield the cis-exo dibromide is unlikely in view of the known preference for trans bromine addition to norbornene.[39] Further support for such an argument is found in the reaction of $Br^\bullet$ with 3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene[107], this reaction giving a mixture of 6-endo-7-exo-dibromo-3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]octane (81 %) and 6-exo-7-exo-dibromo-3,3-diphenyl-exo-tricyclo[3.2.1.$0^{2,4}$]octane (19 %) (Scheme 40b). The role of electron transfer in the reaction of strained systems with bromine has yet to be elucidated.[109]

The preference for Br^+ attack at a double bond can be rationalised from examination of the intermediate carbocation

stabilities, in a manner similar to that developed in Chapter 2c. For electrophilic bromine attack at a cyclopropyl ring, the requirement for the intermediacy of a free classical cation (Chapter 1)[42] (99), can be considered to reflect the relative instability of the initially formed brominated cyclopropane. The free cations formed from bromine attack at a cyclopropyl ring would be expected to be less stable than the delocalised bromonium ions[80] formed from bromine attack at a double bond[39] providing the two species are similarly substituted (Figure 26). Hence, as a consequence of the presence of a non-classical stabilisation for only cation (100), the heat of reaction for electrophilic bromine attack at a double bond will be less than that for the comparative bromination at a cyclopropyl ring and Br^+ attack at a double bond is therefore kinetically favoured over attack at a cyclopropyl ring.

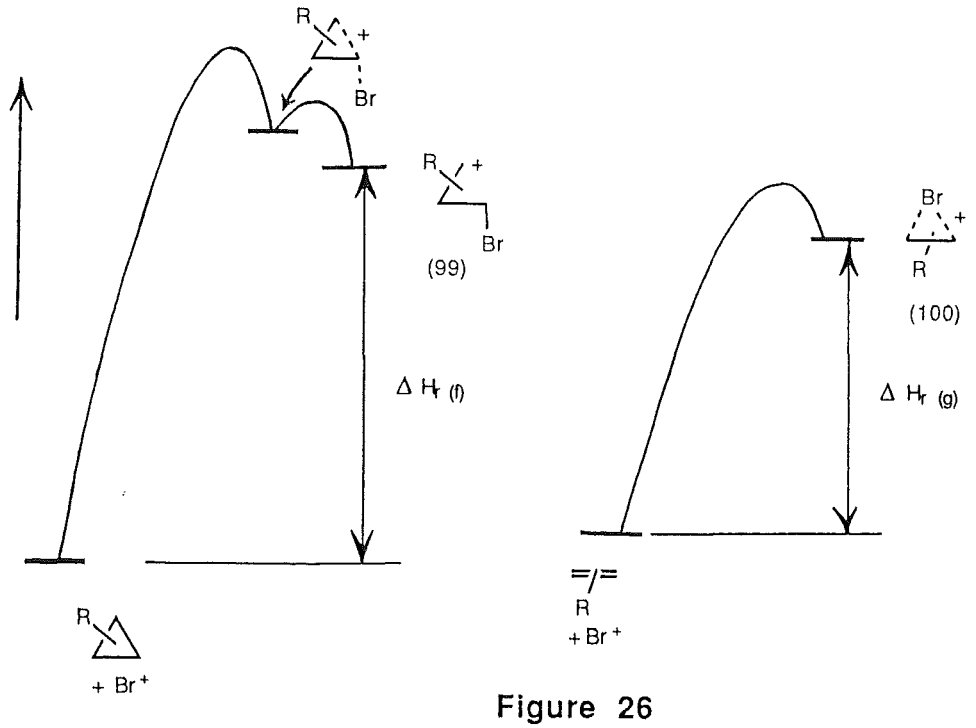
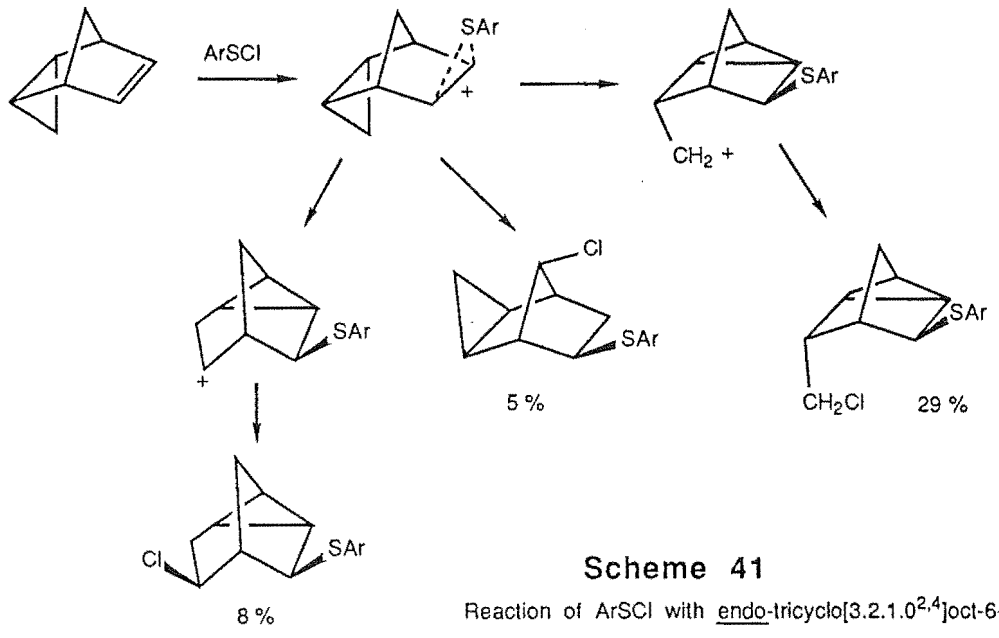


Figure 26

This theory would predict double bond attack for any species which can stabilise an adjacent positive charge resulting from

attack at the double bond, and for which cyclopropyl attack yields no particularly favourable carbocation stabilisation mechanism. Such a result is found in the addition of ArSCl to endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene, where only products resulting from attack of the double bond are reported (Scheme 41).[110] This reflects the ability of the sulphur nucleus to stabilise an adjacent positive charge.[39]



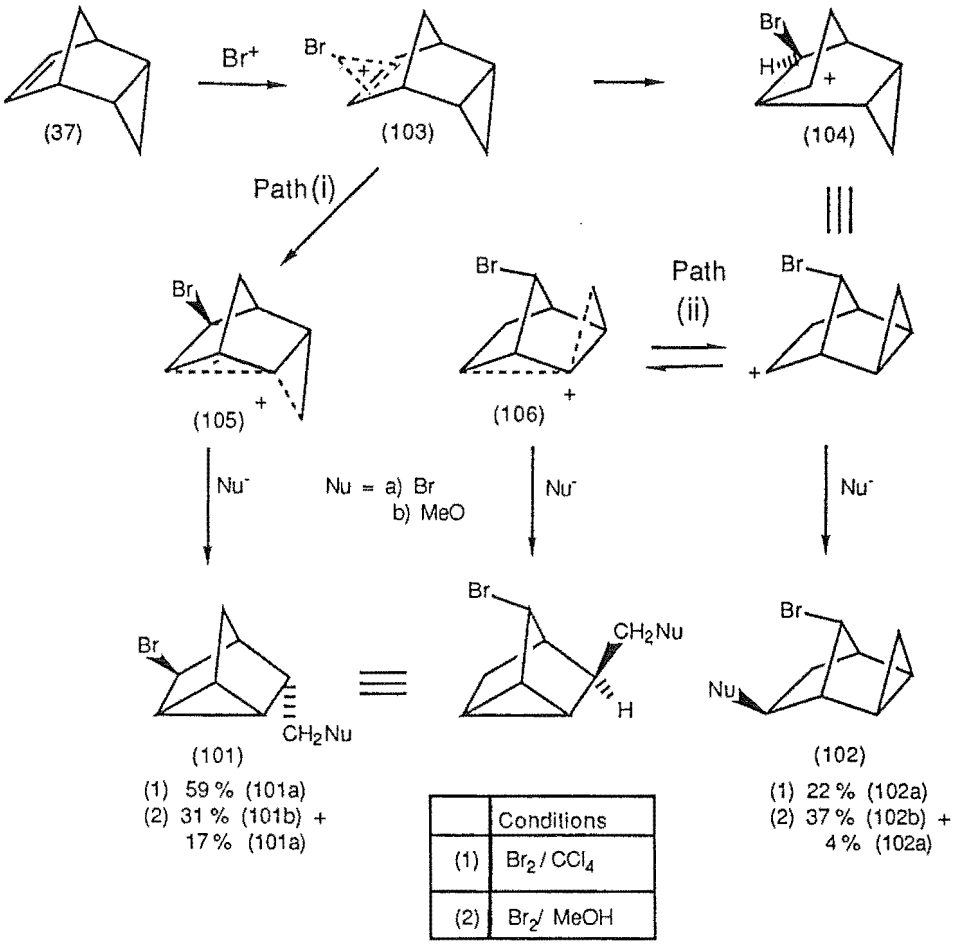
Scheme 41

Reaction of ArSCl with endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene.

C) Bromination of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) with bromine in carbon tetrachloride gave two major products (Scheme 42), subsequently shown to be 5-exo-bromo-3-endo-bromomethyl-tricyclo[2.2.1.$0^{2,6}$]heptane (101a; 59 %) and 6-exo-8-anti-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102a; 22 %) in addition to three minor, unidentified compounds (5 %, 6 % and 7 %). Separation was achieved by radial chromatography.

5-exo-Bromo-3-endo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (101a) was identified from the proton-proton couplings (COSY spectrum). The two carbons substituted with bromine groups, C5 (53.6 ppm) and C8 (32.5 ppm), were assigned from a heteronuclear correlation spectrum, C5 and C8 exhibiting connectivity with H5 at 4.04 ppm and H8a and H8b at 3.23 ppm and 3.12 ppm respectively. The appperance of the C5-H as a



Scheme 42

Reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with Br_2 in 1) CCl_4 2) MeOH.

broad singlet is consistent with the endo stereochemistry. This follows from a comparison with the reported ^{1}H nmr spectra of 5-exo-acetoxy-3-endo-methyltricyclo[2.2.1.$0^{2,6}$]heptane and 5-endo-acetoxy-3-endo-methyltricyclo[2.2.1.$0^{2,6}$]heptane, H5 in the former appearing as a broad singlet, while H5 in the latter

appears as a broad triplet.[111] The stereochemistry of the methylene C8 group was established from a difference NOE spectrum, irradiation at H8a, H8b (3.25-3.10 ppm) giving enhancements at H5 (4.04 ppm, 12.6 %), H4 (2.10 ppm, ca. 1.0 %), H3 (2.04 ppm, 3.2 %) and H2 (1.23 ppm, 2.3 %). The observed couplings between the cyclopropyl protons H1, H2 and H6 ($^3J_{1,2}$ = $^3J_{2,6}$ 5.0 Hz) and the multiplicity of C1, C2 and C6 from an APT spectrum requires the presence of an endocyclic cyclopropyl group.

The identity of 6-exo-8-anti-dibromo-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (102a) follows from the observed proton-proton couplings (COSY spectrum). A heteronuclear correlation spectrum identified the two CHBr groups H6-endo, 3.98 ppm / C6, 47.9 ppm and H8, 3.78 ppm / 47.7 ppm. The presence of an exo-cyclopropyl group was determined by comparison with the coupling and chemical shift data* with exo-tricyclo[3.2.1.$0^{2,4}$]octane (36), (as previously described in Chapter 5b). The endo stereochemistry of the C6-H was established from the couplings to H7-endo (2.33 ppm, 8.0 Hz), H7-exo (2.58 ppm, 4.5 Hz) and H8s (3.78 ppm, 1.5 Hz). Coupling from the C8HBr to H6 (1.5 Hz), H7-endo (2.33 ppm, 1.8 Hz), H1 (2.50 ppm, 1.6 Hz) and H5 (2.79 ppm, 1.6 Hz), in addition to a difference NOE spectrum in which irradiation at H8s (3.78 ppm) gives enhancements at H5 (2.79 ppm, 2.8 %), H1 (2.50 ppm, 2.1 %) and H3-exo (0.78 ppm, 10.7 %) identifies this proton as syn.

To identify the position of attack by electrophilic

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*Footnote: H3endo 0.27 ppm, H3exo 0.78 ppm, H2 0.98 ppm, H4 0.88 ppm, $^2J_{3endo,3exo}$ 7.0 Hz, $^3J_{3endo,2}$ = $^3J_{2,4}$ 7.2 Hz, $^3J_{3endo,4}$ 7.3 Hz, $^3J_{3exo,2}$ = $^3J_{3exo,4}$ 3.2 Hz.

bromine, the reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with bromine in methanol was examined. This reaction gave four products, namely the previously observed 5-exo-bromo-3-endo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (101a; 17 %) and 6-exo-8-anti-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102a; 4 %), along with 5-exo-bromo-3-endo-methoxymethyltricyclo-[2.2.1.$0^{2,6}$]heptane (101b; 31 %) and 8-anti-bromo-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102b; 37 %). Separation was achieved by radial chromatography. For both (101b) and (102b), the magnitude of the coupling between the protons is the same as that observed with the dibromides (101a) and (102a), the only significant differences in the spectra being the chemical shift changes induced by substitution of a bromine with a methoxy.

For 5-exo-bromo-3-endo-methoxymethyltricyclo[2.2.1.$0^{2,6}$]-heptane (101b), a comparison of the chemical shift data* with the dibromide (101a) (Table 14) establishes the methoxy group as being at C8. The endo stereochemistry of the C8H_2-methoxy was confirmed from a difference NOE spectrum, irradiation at H8a, H8b and the methoxy methyl giving enhancements of a singlet at 4.22 ppm assigned to H5-endo (7.4 %), H4 (2.10 ppm, 1.8 %), H3 (1.96 ppm, 5.2 %), H6 (1.52 ppm, 1.2 %) and H2 (1.20 ppm, 2.4 %).

For 8-anti-bromo-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]-octane (102b), comparison of the chemical shift data with that of the corresponding dibromide (102a), (Table 15)* was consistent with the presence of the methoxy group at C6. The endo

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*Footnote: A heteronuclear correlation spectrum identified the carbon-proton connectivities.

Compound	Nucleus	1	2	3	4	5	6	7a	7s	8a	8b
(101a)	^{1}H	1.55	1.23	2.04	2.10	4.04	1.60	2.08	1.38	3.23	3.12
	^{13}C	14.4	19.3	48.1	40.8	53.6	18.3	32.6		32.5	
(101b)	^{1}H	1.44	1.20	1.96	2.10	4.22	1.52	2.13	1.42	3.29	3.25
	^{13}C	13.1	17.0	45.3	39.1	55.4	18.4	32.5		72.3	

Table 14

Comparison of the nmr data (^{1}H and ^{13}C) for dibromo- (101a) and bromo-methoxy- (101b).

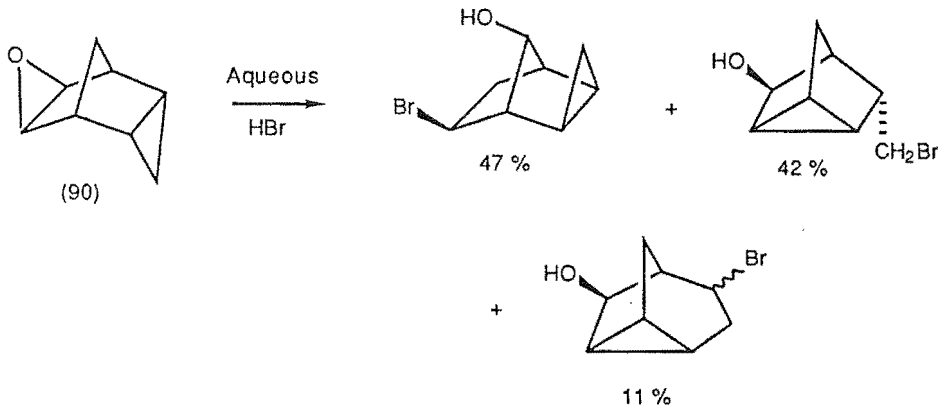
Compound	Nucleus	1	2	3exo	3endo	4	5	6endo	7exo	7endo	8s
(102a)	^{1}H	2.50	0.98	0.78	0.27	0.88	2.79	3.98	2.58	2.33	3.78
	^{13}C	44.4	15.2	4.8		16.4	48.7	47.9	41.8		47.7
(102b)	^{1}H	2.42	0.90	0.76	0.25	0.62	2.67	3.55	2.08	1.98	3.68
	^{13}C	43.8	14.0	5.3		16.1	42.3	84.9	38.4		48.4

Table 15

Comparison of the nmr data (^{1}H and ^{13}C) for dibromo- (102a) and bromo-methoxy- (102b).

stereochemistry of the C6-H follows from coupling to H7-<u>endo</u> (1.98 ppm, $^{3}J_{6\underline{endo},7\underline{endo}}$ 6.4 Hz), H7-<u>exo</u> (2.08 ppm, $^{3}J_{6\underline{endo},7\underline{exo}}$ 3.7 Hz) and H8s (3.68 ppm, $^{4}J_{6\underline{endo},8s}$ 1.6 Hz).

The presence of (101b) and (102b) in the reaction of <u>endo</u>-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with bromine requires initial electrophilic attack at the double bond to give the bromonium ion (103), which can then rearrange to either cation (104) or (105), (Scheme 42). This reaction is mechanistically similar to the reaction of <u>endo</u>-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with ArSCl[110] (Scheme 41) and the reaction of 6-<u>exo</u>-epoxy-<u>endo</u>-tricyclo[3.2.1.$0^{2,4}$]octane with HBr[105,112] (Scheme 43). However the bromination of



(90)

Scheme 43

Reaction of 6-<u>exo</u>-epoxy-<u>endo</u>-tricyclo[3.2.1.$0^{2,4}$]octane (90) with aqueous HBr.

hydrocarbon (37) is unusual in that, unlike the two previously mentioned reactions, no tricyclo[3.2.1.$0^{2,7}$]octanes were observed. To check for the presence of a 4-<u>exo</u> substituted 6-<u>exo</u>-bromotricyclo[3.2.1.$0^{2,7}$]octane (95), the nmr of the crude reaction mixture from the bromination of hydrocarbon (37) was compared with the ^{1}H and ^{13}C nmr spectra of (95a) and (95b) from reaction of hydrocarbon (39) with bromine in either CCl_4 or methanol. There was no evidence for the presence of either (95a) or (95b) in the reaction mixture. This indicates

that interaction of the C2, C4 cyclopropyl bond to give the cation analogous to (98) does not occur in this reaction system.

Conclusions

For electrophilic attack at a cyclopropyl ring, the results of the study reported in this thesis establish that orbital interactions are important for rationalising both the regiochemistry and stereochemistry of reaction. For compounds (34) - (39), the stereochemistry of proton/mercuric acetate attack at the strained ring can be considered to be a result of secondary orbital HOMO/LUMO interactions. The qualitative dependence of electrophilic attack at a cyclopropane ring on frontier molecular orbital interactions is not unexpected. However, only approximately 50 % of the electron density donated to the attacking electrophile (proton) arises from the HOMO (Chapter 1)[29], and even though this orbital is the major contributor of electron density, it is necessary to consider other orbital interactions. Steric factors* for some reactions have been shown to be important. The extent of rearrangement of the protonated and mercurated cyclopropanes determines that cation stability plays a role in dictating reaction pathway. As such, it would be expected that solvent polarity would be of some importance in determining the reaction course. For example, the mercuration of exo-tricyclo[3.2.1.$0^{2,4}$]octane in water gives products from the more stable cation and this is a sufficiently strong driving force to disfavour the reaction which would otherwise occur if HOMO/LUMO interactions controlled the reaction course.

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*Footnote: Perturbation theory or frontier molecular orbital theory do not include a contribution (stabilising or destabilising) from steric strain in the reaction[113], and therefore steric factors must be included separately.

The regiochemistry of electrophilic attack at molecules containing both an alkene and a cyclopropane functionality reflects an importance of the carbocation stabilities of the reaction intermediates. The kinetic preference for protonation at a cyclopropane ring as compared with a double bond, and the preference for bromination at a double bond compared with a cyclopropane, is considered to reflect the stability of the intermediate cations.

The similar stability of the cations from mercuration of a cyclopropane ring and a double bond indicates that mercuration at the various sites is delicately balanced. For example, the mercuration of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) and exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39), gives products from attack at the cyclopropyl ring or the double bond respectively. The preference is rationalised from a consideration of the contribution to the HOMO by the alkene component and the cyclopropyl ring. The more similar in energy the HOMO and the next highest occupied molecular orbital (assigned to the "π" and cyclopropyl e_s orbitals respectively for both (37) and (39)[70a]), the greater will be the cyclopropyl contibution to the HOMO and therefore the less favourable the overlap with the mercury LUMO and the pi component of the HOMO. Such a reduction in overlap is enough to allow cation stabilities to dictate the reaction pathway for mercuration of hydrocarbon (37), the mercurated cyclopropane (53c) being stabilised relative to the comparable mercurinium ion from attack at the double bond. For hydrocarbon (39), the large contribution of the pi component to the HOMO, a consequence of the large energy separation between the HOMO and the next highest occupied molecular orbital, gives rise to predominant mercuric acetate attack at the double bond.

The results in this qualitative study serve to highlight the complex nature of electrophilic attack at a cyclopropyl ring, with a number of factors determining the reaction pathway. To accurately quantitate these reactions, ab initio molecular orbital calculations (see for example reference 29) become essential. However, to quote R. Hoffmann[114], "To understand an observable means to me being able to predict, albeit qualitatively, the result that a perfectly reliable calculation would yield for that observable." Hence, if utilisation of the reactions of cyclopropane rings with electrophiles is to be of any great use, then the practising chemist must have access to a readily usable theory. However, the very complexity of these reactions may mean that any such theory is at best limited, and complete ab initio molecular orbital calculation will be necessary for certain predictive analyses.

Experimental Section

General Methods

Nmr spectra were obtained on a Varian T-60 or Varian XL-300 (300 MHz ^{1}H, 75 MHz ^{13}C, 46 MHz ^{2}H). All ^{2}H nmr spectra were run unlocked with broadband proton decoupling, an acquisition time of 4s and using 2 drops of $CDCl_3$ (δ 7.27 ppm) as an internal reference. Heteronuclear proton-carbon correlation spectra were obtained using a relaxation time of 4s between scans, 64 values of t_1, and zero filling to 256 points in f_1 (^{1}H). NOE's were obtained by difference spectra, the decoupler offset for the reference spectrum being 10,000 Hz. A delay time of 20 s was incorporated to ensure complete relaxation, along with a line broadening of 1 Hz and an acquisition time of 1.5 s with zero filling to 16384 points. Mass spectra were run on AEI MS902 spectrometer. A Hewlett Packard HP 5890A glc was used in both analytical and preparative modes. For preparative separations 1.5 % OV-17 and 1.95 % QF-1 on chromosorb W in a column of 5mm external diameter and length 3m was used. Unlesss otherwise stated all preparative separations employed this column. Radial chromatography was performed on a Chromatatron (Harrison and Harrison) using Merck type 60 $P.F._{254}$ silica gel.

endo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37)

endo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) was prepared from the reaction of cyclopropene with cyclopentadiene at -78°C.[59] The ^{1}H nmr and ^{13}C nmr are as reported.[59b,115]

endo-Tricyclo[3.2.1.$0^{2,4}$]octane (34)

To a suspension of activated palladium on carbon (5 %; 80 mg) in pentane was added endo-tricyclo[3.2.1.$0^{2,4}$]-oct-6-

ene (37)[59] (1 g) in pentane (20 ml). The mixture was stirred vigorously in a hydrogen atmosphere until one mole of hydrogen had been adsorbed. The mixture was filtered and the solvent removed by distillation through a Vigreux column. The residual liquid was left in an open flask for a few hours to remove the remaining traces of pentane to give endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) (0.90 g, 90%) as a low melting glass, m.p. 71-72°. ^{1}H nmr δ_H ($CDCl_3$) 2.21 (s), $W_{h/2}$ 7 Hz, H1, H5; 1.88 (m), $^{2}J_{8s,8a}$ 8.3 Hz, $^{3}J_{8s,1}$ = $^{3}J_{8s,5}$ = $^{3}J_{8s,6endo}$ = $^{3}J_{8s,7endo}$ 2.1 Hz, H8s; 1.44 (d of d), $^{2}J_{8a,8s}$ 8.3 Hz, $^{5}J_{8a,3exo}$ 2.4 Hz, H8a; 1.36 - 1.30 (m), H2, H4, H6exo, H7exo; 1.01 (d of d), $^{2}J_{6endo,6exo}$ 7.3 Hz, $^{3}J_{6endo,7exo}$ 2.3 Hz, H6endo, H7endo; 0.88 (d of t), $^{2}J_{3endo,3exo}$ 5.9 Hz, $^{3}J_{3endo,2}$ = $^{3}J_{3endo,4}$ 2.4 Hz, H3endo; 0.72 (m), $^{2}J_{3exo,3endo}$ 5.9 Hz, $^{3}J_{3exo,2}$ = $^{3}J_{3exo,4}$ 7.4 Hz, $^{5}J_{3exo,8a}$ 2.3 Hz, H3exo. ^{13}C nmr as published.[88,116]

exo-Tricyclo[3.2.1.$0^{2,4}$]octane (36)

exo-Tricyclo[3.2.1.$0^{2,4}$]octane (36) was prepared from norbornene by addition of methylene carbene generated using a zinc / copper couple.[61] ^{1}H nmr δ_H ($CDCl_3$) 2.21 (s), $W_{h/2}$ 5.1 Hz, H1, H5; 1.43, $W_{h/2}$ 18 Hz, H6exo, H7exo; 1.24, $W_{h/2}$ 13 Hz, H6endo, H7endo; 0.92 (d of t), $^{2}J_{8s,8a}$ 10.4 Hz, $^{4}J_{8s,6endo}$ = $^{4}J_{8s,7endo}$ 2.1 Hz, H8s; 0.66 (d of d), $^{3}J_{2/4,3endo}$ 7.3 Hz, $^{3}J_{2/4,3exo}$ 3.2 Hz, H2, H4; 0.57 (d), $^{2}J_{8a,8s}$ 10.4 Hz, H8a; 0.28 (d of t), $^{2}J_{3exo,3endo}$ 6.0 Hz, $^{3}J_{3exo,2}$ = $^{3}J_{3exo,4}$ 3.1 Hz, H3exo.; -0.11 (m), $^{2}J_{3endo,3exo}$ 6.1 Hz, $^{3}J_{3endo,2}$ = $^{3}J_{3endo,4}$ 7.0 Hz, H3endo. Partial assignments of the ^{1}H nmr for this compound have previously been published.[117] ^{13}C nmr as published.[88]

exo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39)

exo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) was prepared by the addition of methylene carbene to norbornadiene[63] using the zinc / copper couple of LeGoff.[61] The ^{1}H nmr and ^{13}C nmr are as reported.[59b,78,88,118]

2-Methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38)

1-Methylcyclopropene[60] was bubbled with N_2 into a solution of cyclopentadiene (30 g) in methylene chloride (50 ml) at -78°. Generation of 1-methylcyclopropene was maintained for 6 hrs. The solvent was removed by distillation through a Vigreux column and the residue purified by distillation through a spinning band distillation column to give 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38): ^{1}H nmr δ_H ($CDCl_3$) 5.88 (d of d), $^{3}J_{7,1}$ 3.5 Hz, $^{3}J_{7,6}$ 5.5 Hz, H7; 5.68 (d of d), $^{3}J_{6,7}$ 5.5 Hz, $^{3}J_{6,5}$ 3.2 Hz, H6; 2.84 (s), $W_{h/2}$ 8 Hz, H5; 2.44 (s), $W_{h/2}$ 6 Hz, H1; 1.92 (d of t), $^{2}J_{8s,8a}$ 6.8 Hz, $^{3}J_{8s,5} = {}^{3}J_{8s,1}$ 1.8 Hz, H8s; 1.65 (d of d), $^{2}J_{8a,8s}$ 6.8 Hz, $^{5}J_{8a,3exo}$ 2.0 Hz, H8a; 1.32 (s), $W_{h/2}$ 2Hz, CH_3; 1.00 (d of t), $^{3}J_{3endo,3exo}$ 7.0 Hz, $^{3}J_{3endo,4} =$ J 3.5 Hz, H3endo; 0.56 (d of d), $^{2}J_{4,3endo}$ 3.1 Hz, $^{3}J_{4,3exo}$ 5.1 Hz, H4; 0.48 (m), $^{2}J_{3exo,3endo}$ 7.2 Hz, $^{3}J_{3exo,4}$ 5.1 Hz, $^{5}J_{3exo,8a}$ 2.6 Hz, H3exo. ^{13}C nmr as published.[78]

2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35)

To a suspension of activated palladium on carbon (5 %, 80 mg) in pentane was added 2-methyl-endo-tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene (38) (1 g) in pentane (30 ml). The mixture was stirred in a hydrogen atmosphere until one molar equivalent of hydrogen had been adsorbed. The mixture was

filtered and the solvent removed by distillation through a Vigreux column. The residual liquid was left in an open flask for a few hours to remove the last traces of pentane to give 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (0.76 g, 76 %) as a colourless oil. ^{1}H nmr δ_H ($CDCl_3$) 2.26 (s), $W_{h/2}$ 9 Hz, H5; 1.97 (s), $W_{h/2}$ 7 Hz, H1; 1.92 (m), $^{2}J_{8s,8a}$ 8.3 Hz, $^{3}J_{8s,1}$ = $^{3}J_{8s,5}$ = $^{4}J_{8s,6endo}$ = $^{4}J_{8s,7endo}$ 2.2 Hz, H8s; 1.38 - 1.27, H8a, H6exo, H7exo; 1.15 (s), Me; 1.10 - 0.95, H6endo, H7endo, H4, H3endo; 0.56 (m), $^{2}J_{3exo,3endo}$ 7.8 Hz, $^{3}J_{3exo,4}$ 5.6 Hz; $^{5}J_{3exo,8a}$ 2.2 Hz, H3exo. The following assignments were obtained from a heteronuclear correlation experiment: 1.33, H8a; 1.32, H6exo; 1.28, H7exo; 1.07, H6endo; 1.00, H4, H7endo; 0.94, H3endo. ^{13}C nmr δ_C ($CDCl_3$) 50.8, C8; 42.3, C1; 38.3, C5; 29.8, C4; 27.1, C6; 26.2, C7; 24.3, C3; 22.5, Me; C2 not obs.

Reaction of (34) with p-toluenesulphonic acid, methanol

endo-Tricyclo[3.2.1.$0^{2,4}$]octane (34) (120 mg), anhydrous methanol (3 ml) and p-toluenesulphonic acid monohydrate (8 mg) were placed in an ampoule (5 ml) and kept at 80°C for 7 days. The mixture was diluted with water (5 ml) and the product extracted into pentane. The pentane extracts were washed with aqueous sodium carbonate solution, dried over $MgSO_4$ and the solvent removed under reduced pressure to give an oil (130 mg, 81 %) shown by glc analysis to be at least 95 % pure and shown to be 2-endo-methoxybicyclo[3.2.1]octane (40a): ^{1}H nmr δ_H ($CDCl_3$) 3.30 (s), OMe; 3.18, $^{3}J_{2exo,3endo}$ 10.1 Hz, $^{3}J_{2exo,3exo}$ 5.7 Hz, $^{3}J_{2exo,1}$ 3.0 Hz, H2exo; 2.36, $^{3}J_{1,2exo}$ 3.0 Hz, $^{3}J_{1,7exo}$ 6.0 Hz, $^{3}J_{1,8a}$ 6.0 Hz, H1; 2.12 (s), $W_{h/2}$ 7 Hz, H5; 1.9 - 1.2 (m, 10 H's). The following asignments were obtained from a heteronuclear correlation experiment: 1.82, H3exo; 1.73, H7exo; 1.65, H6exo; 1.59, H8a;

1.50, H7endo; 1.41, H4endo; 1.34, H6endo; 1.33, H4exo; 1.28, H8s; 1.23, H3endo. ^{13}C nmr δ_C ($CDCl_3$) 81.9, C2; 55.7, OMe; 38.6, C1; 37.5, C8; 34.4, C5; 31.0, C4; 28.8, C6; 25.7, C3; 23.9, C7.

Preparation of 2-endo-methoxybicyclo[3.2.1]octane and (47b)

A solution of 3-bromobicyclo[3.2.1]oct-3-en-2-exo-ol (44)[119] (4 g) in tetrahydrofuran (30 ml) with aqueous sodium hydroxide (30 ml, 1M) was shaken with prehydogenated palladium on carbon (2.4 g, 10 %) under hydrogen at 1.5 atmospheres. After the addition of hydrogen was complete, the mixture was diluted with water, saturated with NaCl, and the product extracted with ether. The solvent was removed by distillation and the crude product steam distilled to give bicyclo[3.2.1]octan-2-exo-ol[26] (1.88 g, 75 %) as a white solid. ^1H nmr δ_H ($CDCl_3$) 3.73 (s), $W_{h/2}$ 8 Hz, H2; 2.21, H1; 2.16, H5; 1.92 (d), $^2J_{8s,8a}$ 10.0 Hz, H8s; 1.75 (s), $W_{h/2}$ 3 Hz, OH; 1.69 (m), H4exo, H6exo, H7exo, H3exo; ca. 1.5, H7endo; 1.39 (m), H6endo, H3endo; 1.26 (m), H4endo; 1.19 (m), H8a. The position of H4exo was obtained by an NOE experiment using the alcohol -OD. ^{13}C nmr δ_C ($CDCl_3$) (revised from reference 64) 71.3, C2; 41.6, C1; 34.3, C5; 32.1, C8; 28.3, C4; 26.8, C7; 26.7, C6; 26.4, C3.

The reaction of 3-bromobicyclo[3.2.1]oct-3-en-2-exo-ol (44) (4g) was repeated using deuterium, NaOD and D_2O to give 3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-exo-ol (45) (1.6g, 63%): ^2H nmr δ_D ($CHCl_3$) 1.64 (2 D), D3exo, D4exo; 1.38 (1 D), D3exo; 1.25 (0.34 D), D4endo. ^{13}C nmr δ_C ($CDCl_3$) 71.2 (L.B.), C2; 41.5, C1; 34.1 (L.B.), C5; 32.0, C8; 27.6, t, $J_{^{13}C,^2H}$ 18.7 Hz, C4; 26.7, C7; 26.6 (L.B.), C6; 25.8 (m), C3. (L.B.) indicates the presence of a small ^{13}C-^2H coupling.[120]

Bicyclo[3.2.1]octan-2-exo-ol (1.54 g) was oxidised by chromium trioxide in acetic acid[121] to give bicyclo[3.2.1]octan-2-one (1.2 g, 79 %) as a white solid. ^{1}H nmr δ_H ($CDCl_3$) 2.69 (t), $^{3}J_{1,7exo} = {}^{3}J_{1,8a}$ 4.6 Hz, H1; 2.44 (m), H5; 2.37 (m), H3exo; 2.19 (q), $^{2}J_{3endo,3exo}$ 16.0 Hz, $^{3}J_{3endo,4endo}$ 7.0 Hz, H3endo; ca. 2.0, H6exo; ca. 1.8, H4endo, H4exo, H7exo, H7endo; ca. 1.7, H6endo. ^{13}C nmr: as published.[64]

3,3,4-exo-Trideuterobicyclo[3.2.1]octan-2-one (46) was prepared as above but by oxidation with chromium trioxide in deuteroacetic acid. ^{13}C nmr δ_C ($CDCl_3$) 210.9, C2; 51.1, C1; 38.2, C8; 33.8 (L.B.), C5; 31.6, t, $J_{^{13}C,^{2}H}$ 19.4 Hz, C4; 28.0, C7; 27.9 (L.B.), C6. ^{2}H nmr δ_D ($CHCl_3$) 2.33 (0.92 D), D3exo; 2.16 (0.88 D), D3endo; 1.77 (0.28 D) D4endo; 1.69 (0.73 D), D4exo. Mass spectrum shows 3 % D^0, 5 % D^1, 22 % D^2, 61 % D^3, 6 % D^4, 1 % D^5, 6 % D^6.

To 3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-one (46) (100 mg) in anhydrous ether (10 ml) was added with stirring, $LiAlH_4$ (140 mg). After stirring for 3 hours, the excess $LiAlH_4$ was destroyed by the careful addition of sodium sulphate decahydrate crystals. Water (10 ml) was added and the aqueous layer extracted with ether. The combined ether extracts were washed with a brine solution and dried over Na_2SO_4. Removal of the solvent at reduced pressure gave a mixture (4:1; 82 mg, 81 %) of 3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-endo-ol (47a): ^{13}C nmr δ_C ($CDCl_3$) 72.4, C2; 42.5, C1; 37.1, C8; 33.4, C5; 30.0, t, $J_{^{13}C,^{2}H}$ 20.0 Hz, C4; 28.4, C6; 23.2, C7; C3, not obs. ^{2}H nmr δ_D ($CHCl_3$) 1.74 (0.85 D); 1.67 (0.3 D), D4endo; 1.35 (0.90 D); 1.24 (0.75 D); and 3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-exo-ol (45).

3,3,4-exo-Trideuterobicyclo[3.2.1]octan-2-endo-ol (47a) (94 mg) in dry benzene (5 ml) was added dropwise with vigorous stirring, to sodium amide (200 mg) in dry benzene (5 ml). The mixture was heated under reflux for 16 hours and the benzene removed by draining the water out of the condensor. Methyl iodide (3.4 g, 1.5 ml) in anhydrous ether (5 ml) was added and the mixture heated under reflux for 8 hours. Water (10 ml) was carefully added and the ether layer separated. The aqueous layer was extracted with ether, the combined ether extracts washed with a brine solution, and dried over $MgSO_4$. Removal of the solvent at reduced pressure gave 2-endo-methoxy-3,3,4-exo-trideuterobicyclo[3.2.1]octane (47b) (48 mg, 47 %) as a pale yellow oil. ^1H nmr δ_H ($CDCl_3$) 3.30, OMe; 3.16, $W_{h/2}$ 6 Hz, H2; 2.35, $^4J_{1,5}$ 2.1 Hz, $^3J_{1,8a}$ 6.1 Hz, $^3J_{1,7exo}$ 6.1 Hz, H1; 2.10 (s), $W_{h/2}$ 15.8 Hz, H5; 1.85 - 1.20, (m), (7.2 H). ^{13}C nmr δ_C ($CDCl_3$) 81.8, C2; 55.6, OMe; 38.5, C1; 37.4, C8; 34.3, C5; 30.4, t, $J_{^{13}C,^2H}$ 19.1 Hz, C4; 28.8, C6; 23.9, C7; C3, not observed. ^2H nmr δ_D ($CHCl_3$) 1.78 (0.90 D), D3exo; 1.42 (0.25 D), D4endo; 1.33 (0.71 D), D4exo; 1.23 (0.90 D), D3endo.

Reaction of (34) with mercuric acetate

To a solution of endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) (100 mg) in anhydrous methanol (4 ml) was added, with stirring, mercuric acetate (300 mg) and the mixture stirred for 3 hours. The mixture was filtered to remove unreacted mercuric acetate, the solvent removed under reduced pressure and the organomercurial placed under high vacuum for 12 hours to remove acetic acid. The residue, a pale green viscous oil was identified as 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]octane (40c) (275 mg, 95 %). ^1H nmr δ_H ($CDCl_3$) 3.40 (s), OMe; 3.18 (m),

$^{3}J_{2\underline{exo},1}$ 2.6 Hz, $^{3}J_{2\underline{exo},3\underline{exo}}$ 5.4 Hz, $^{3}J_{2\underline{exo},3\underline{endo}}$ 9.8 Hz, H2exo; 2.75 (q of t), $^{3}J_{4\underline{exo},3\underline{endo}}$ 13.6 Hz, $^{3}J_{4\underline{exo},3\underline{exo}}$ 4.7 Hz, $^{3}J_{4\underline{exo},5}$ 1.7 Hz, $^{4}J_{4\underline{exo},6\underline{exo}}$ 1.6 Hz, $J_{^{199}Hg,H4}$ 192 Hz, H4; 2.50 (t), $^{3}J_{5,6\underline{exo}} = {}^{3}J_{5,8a}$ 6.0 Hz, H5; 2.33 (s), $W_{h/2}$ 11.9 Hz, H1; 2.25 (m) H6exo; 2.00 (s) OAc; 1.9-1.75 (m) H7exo, H3exo, H6endo; 1.68 (m), $^{2}J_{8s,8a}$ 12.0 Hz, $^{3}J_{8a,1} = {}^{3}J_{8a,5}$ 5.0 Hz; H8a; 1.55 (m) H3endo, H7endo; 1.38 (d), $^{2}J_{8a,8s}$ 12.0 Hz, H8s. ^{13}C nmr δ_C (CD_3OD) 178.4, OAc; 82.5, $J_{^{199}Hg,^{13}C}$ 310 Hz, C2; 55.7, OMe; 50.3, $J_{^{199}Hg,^{13}C}$ 1634 Hz, C4; 40.8, $J_{^{199}Hg,^{13}C}$ 66 Hz, C5; 39.3, $J_{^{199}Hg,^{13}C}$ 25 Hz, C1; 38.8, $J_{^{199}Hg,^{13}C}$ 310 Hz, C8; 32.7, $J_{^{199}Hg,^{13}C}$ 65 Hz, C6; 31.2, $J_{^{199}Hg,^{13}C}$ 97 Hz, C3; 23.8, $J_{^{199}Hg,^{13}C}$ not obs., C7; 22.9, OAc. Note: The $^{199}Hg,^{13}C$ coupling constants are the averages obtained from three separate spectra.

Reaction of (34) with methanol-d_1, p-toluenesulphonic acid

The reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) (120 mg) with methanol-d_1 was carried out as previously described for the reaction with methanol. The product was isolated after 7 days to give 4-endo- and 6-endo-deutero-2-endo-methoxybicyclo[3.2.1]octane (40b and 41b) (120 mg, 79 %) in the ratio of 62:38 ($\pm$ 4 %) respectively. Mass spectrum shows 15 % D^o; 84% D^1; 1 % D^2. $C_9H_{15}OD$ requires $M^{+\cdot}$ 141.1264; Found $M^{+\cdot}$ 141.1269. ^{2}H nmr δ_D ($CHCl_3$) 1.41, D4endo; 1.34, D6endo.

4-endo-Deutero-2-endo-methoxybicyclo[3.2.1]octane (40b): ^{13}C nmr δ_C ($CDCl_3$) 81.6, C2; 55.4, OMe; 38.4, C1; 37.2, C8; 34.1, C5; 30.3, t, $J_{^{13}C,^{2}H}$ 20.4 Hz, C4; 28.5, C6; 25.3, C3; 23.6, C7. 6-endo-Deutero-2-endo-methoxybicyclo[3.2.1]octane (41b): ^{13}C nmr δ_C ($CDCl_3$) 81.6, C2; 55.4, OMe; 38.4, C1; 37.2, C8;

34.1, C5; 30.7, C4; 28.2, t, $J_{^{13}C,^{2}H}$ 19.9 Hz, C6; 25.4, C3; 23.5, C7.

Reduction of the organomercurial (40c) with:

(a) Sodium borohydride.

To the crude 4-endo-acetoxymercurio-2-endo-methoxy-bicyclo[3.2.1]octane (40c) (275 mg) in methanol (4 ml) was added with stirring, aqueous NaOH (5 ml, 1M), followed by a solution of NaOH (5 ml, 1M) and sodium borohydride (80 mg). After 30 minutes the mixture was extracted with pentane, washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure to give 2-endo-methoxy-bicyclo[3.2.1]octane (40a) (68 mg, 66 %), identical to a sample obtained by the reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (34) with toluenesulphonic acid in methanol.

(b) Sodium borodeuteride.

To the crude 4-endo-acetoxymercurio-2-endo-methoxy-bicyclo[3.2.1]octane (40c) (100 mg) dissolved in methanol (1 ml) was added with stirring, aqueous NaOH (1 ml, 1M), and sodium borodeuteride (20 mg). After 30 minutes stirring, the liquid was extracted with pentane, washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure to give a mixture (45:55; 25 mg, 65 %) shown to be 4-exo- and 4-endo- deutero-2-endo-methoxybicyclo[3.2.1]octane respectively. ^{2}H nmr δ_D ($CHCl_3$) 1.40, D4endo; 1.33, D4exo. Mass spectrum shows 6 % D^o; 94 % D^1;

(c) Sodium mercury amalgam.

Mercury (50 g) was cautiously added dropwise to molten sodium (0.75 g) under Shell Ondina 17 (20 ml). The resulting amalgam was left to cool before being transferred to a mortar where it was broken into small pieces under pentane. To the

sodium mercury amalgam (5g, 1.5 %), previously washed with pentane and dried under vacuum for 1 hour, in NaOD, D_2O (2ml, 2M) was added the organomercurial (40c) (100 mg). The mixture was stirred for 3 hours and water (4 ml) added. The mixture was extracted with pentane, the combined extracts dried over $MgSO_4$ and the solvent removed under reduced pressure to give 4-endo-deutero-2-endo-methoxybicyclo[3.2.1]octane (40b) (23 mg, 64 %) as an oil. ^2H nmr δ_D ($CHCl_3$) 1.39, D4endo. ^{13}C nmr δ_C ($CDCl_3$) 81.6, C2; 55.4, OMe; 38.4, C1; 37.2, C8; 34.1, C5; 30.3, t, C4, $J_{^{13}C-^2H}$ 20.4 Hz; 28.5, C6; 25.3, C3; 23.6, C7; Mass spectrum shows 6 % D^o; 94 % D^1.

Reaction of (37) with mercuric acetate, methanol

To a solution of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37), (200 mg) in anhydrous methanol (4 ml) was added, with stirring, mercuric acetate (600 mg) and the mixture stirred at room temperature overnight. The solvent and acetic acid were removed under reduced pressure to give a colourless oil (795 mg, 95 %) subsequently shown to contain 4-endo-acetoxymercurio-2endo-methoxybicyclo[3.2.1]oct-6-ene (50c) (ca. 75 %) and 6- and 7-endo- acetoxymercurio-2-endo-methoxybicyclo[3.2.1]oct-3-ene (52c and 51c) (ca. 10 % and ca. 11 % respectively).

4-endo-Acetoxymercurio-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50c): ^1H nmr δ_H ($CDCl_3$) 6.08 (d of d), $^3J_{7,6}$ 5.5 Hz, $^3J_{7,1}$ 2.5 Hz, H7; 6.02 (d of d), $^3J_{6,7}$ 5.7 Hz, $^3J_{6,5}$ 2.5 Hz, H6; 3.30, OMe; 3.26 (m), $^3J_{2exo,1}$ 3.2 Hz, $^3J_{2exo,3endo}$ 9.5 Hz, $^3J_{2exo,3exo}$ 6.0 Hz, H2exo; 2.88 (d of t), $^3J_{5,4exo}$ = $^4J_{5,6}$ 2.5 Hz, $^3J_{5,8a}$ 5.2 Hz, H5; 2.77 (d of t), $^3J_{1,2exo}$ 3.0 Hz, $^3J_{1,7}$ 2.0 Hz, $^3J_{1,8a}$ 3.6 Hz, H1; 2.73 (m), $^3J_{4exo,3exo}$ 5.6 Hz, $^3J_{4exo,3endo}$ 12.3 Hz, $^3J_{4exo,5}$ 2.0 Hz,

H4exo; 2.26 (d of t), $^{2}J_{3exo,3endo}$ 13.1 Hz, $^{3}J_{3exo,4exo}$ = $^{3}J_{3exo,2exo}$ 5.6 Hz, H3exo; 2.13 (d of t), $^{2}J_{8a,8s}$ 11.1 Hz, $^{3}J_{1,8a}$ = $^{3}J_{5,8a}$ 5.6 Hz, H8a; 2.02, OAc; 1.95 (d of t), $^{2}J_{3endo,3exo}$ = $^{3}J_{3endo,4exo}$ 12.8 Hz, $^{3}J_{3endo,2exo}$ 9.5 Hz, H3endo; 1.30 (d), $^{2}J_{8a,8s}$ 10.7 Hz, H8s. ^{13}C nmr δ_C ($CDCl_3$) 176.8, OAc; 133.6, C6; 132.4, C7; 80.0, C2; 55.8, OMe; 44.6, C5; 43.3, C8; 43.1, C1; 42.1, C4; 32.3, C3; 23.0, OAc.

Reduction of the organomercurials (50c, 51c and 52c) with sodium,mercury amalgam

The reduction was carried out as outlined in the reduction of 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]octane (40c) above. The reduction of the products from the reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) with mercuric acetate in methanol gave a mixture (23 mg, 64 %) of 6-endo- and 7-endo- deutero-2-exo-methoxybicyclo[3.2.1]oct-3-ene (52b and 51b) (10 % and 11 % respectively) and 4-endo-deutero-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50b) (75 %), identical to that obtained from the acid catalysed reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) with methanol-d_1. The 6-endo- and 7-endo- deutero-2-exo-methoxybicylo[3.2.1]oct-3-ene (52b and 51b) and 4-endo-deutero-2-endo-methoxybicyclo-[3.2.1]oct-6-ene (50b) were separated by preparative glc. 4-endo-Deutero-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50b): ^{1}H nmr δ_H ($CDCl_3$) 5.92 (d of d), $^{3}J_{6,7}$ 5.8 Hz, $^{3}J_{6,5}$ 2.2 Hz, H6; 5.86 (d of d), $^{3}J_{7,6}$ 5.8 Hz, $^{3}J_{7,1}$ 2.2 Hz, H7; 3.34, OMe; 3.19 (m), $^{3}J_{2exo,3endo}$ 9.3 Hz, $^{3}J_{2exo,1}$ 2.7 Hz, $^{3}J_{2exo,3exo}$ 5.6 Hz, H2exo; 2.82 (d of t), $^{3}J_{1,2exo}$ 2.7 Hz, $^{3}J_{1,7}$ 2.6 Hz, $^{3}J_{1,8a}$ 5.5 Hz, H1; 2.50 (d of t), $^{3}J_{5,4exo}$ = $^{3}J_{5,6}$ 2.6 Hz, $^{3}J_{5,8a}$ 5.5 Hz, H5; 2.02 (d of t), $^{2}J_{8a,8s}$ 10.3 Hz, $^{3}J_{8a,1}$ = $^{3}J_{8a,5}$ 5.5 Hz, H8a; 1.84 (d of t),

$^{2}J_{3\underline{exo},3\underline{endo}}$ 13.0 Hz, $^{3}J_{3\underline{exo},2\underline{exo}}$ 5.6 Hz, $^{3}J_{3\underline{exo},4\underline{exo}}$ 6.2 Hz, H3exo; 1.42 (m), $^{2}J_{3\underline{endo},3\underline{exo}}$ 13.0 Hz, $^{3}J_{3\underline{endo},2\underline{exo}}$ 9.3 Hz, $^{3}J_{3\underline{endo},4\underline{exo}}$ 11.6 Hz, H3endo; 1.32, H4exo; 1.28 (d), $^{2}J_{8a,8s}$ 10.3 Hz, H8s. ^{13}C nmr δ_C ($CDCl_3$) 133.8, C6; 130.3, C7; 76.4, C2; 55.4, OMe; 42.4, C1; 41.9, C8; 38.9, C5; 25.3, C3; 22.9, t, $J_{^{13}C,^{2}H}$ 19.5 Hz, C4. The ^{13}C nmr of 2-endo-methoxybicyclo[3.2.1]oct-6-ene (50a) was assigned by comparison with the corresponding bicyclo[3.2.1]oct-6-en-2-endo-ol.[122] ^{2}H nmr δ_D ($CHCl_3$) 1.34, D4endo. Mass spectrum shows 1 % D^o; 95 % D^1; 4 % D^2.

Computer simulations using the FORTRAN LAME program[77] for 4-endo-deutero-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50b) gave excellent agreement with the observed ^{1}H nmr spectrum for the following values: linewidth 1.2 Hz; 3.19 ppm, $^{3}J_{2\underline{exo},3\underline{endo}}$ 9.3 Hz, $^{3}J_{2\underline{exo},3\underline{exo}}$ 5.6 Hz, $^{3}J_{2\underline{exo},1}$ 2.7 Hz, H2exo; 2.80 ppm, $^{3}J_{1,2\underline{exo}}$ 2.7 Hz, $^{3}J_{1,7}$ 2.6 Hz, $^{3}J_{1,8a}$ 5.5 Hz, H1; 2.50 ppm, $^{3}J_{5,4\underline{exo}} = {}^{3}J_{5,6}$ 2.6 Hz, $^{3}J_{5,8a}$ 5.5 Hz, H5; 2.02 ppm, $^{3}J_{8a,1} = {}^{3}J_{8a,5}$ 5.5 Hz; $^{2}J_{8a,8s}$ 10.3 Hz, H8a; linewidth 2.2 Hz; 1.83 ppm, $^{2}J_{3\underline{exo},3\underline{endo}}$ 13.0 Hz, $^{3}J_{3\underline{exo},2\underline{exo}}$ 5.6 Hz, $^{3}J_{3\underline{exo},4\underline{exo}}$ 6.2 Hz, H3exo; 1.42 ppm, $^{2}J_{3\underline{endo},3\underline{exo}}$ 13.0 Hz, $^{3}J_{3\underline{endo},2\underline{exo}}$ 9.3 Hz, $^{3}J_{3\underline{endo},4\underline{exo}}$ 11.6 Hz, H3endo; 1.32 ppm, $^{3}J_{4\underline{exo},3\underline{endo}}$ 11.6 Hz, $^{3}J_{4\underline{exo},3\underline{exo}}$ 6.2 Hz, H4exo. Note: H4exo is present only to induce second order effects at H3endo (1.42 ppm), and consequently does not give an accurate simulation in this part of the spectrum.

6-endo- and 7-endo- Deutero-2-exo-methoxybicyclo[3.2.1]oct-3-ene (52b and 51b): ^{1}H nmr, ^{2}H nmr and ^{13}C nmr as reported.[75]

Reaction of (37) with deutero-methanol catalysed by acid

The reaction was carried out as described previously.[75] Repetitive preparative glc gave

4-endo-deutero-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50b), whose ^{1}H nmr was identical to that obtained from the sodium mercury amalgam reduction of 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]oct-6-ene (50c) above. All spectral data are supplied in the sodium, mercury reduction of the crude organomercurials from the reaction of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) with mercuric acetate, methanol above.

Reaction of (36) with p-toluenesulphonic acid, methanol at 80°C

Reaction of exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) (150 mg) with methanol, p-toluenesulphonic acid was carried out as previously described for the reaction with endo-tricyclo[3.2.1.$0^{2,4}$]octane (34). The product was isolated after 7 days to give an oil (174 mg, 89 %), shown by glc to contain 3 compounds (15 %, 9 %, 76 %). Separation was achieved by preparative glc. 2-exo-Methoxybicyclo[3.2.1]octane (62a) (76 %): ^{1}H nmr δ_H ($CDCl_3$) 3.30 (s), OMe; 3.18, $W_{h/2}$ 8 Hz, H2endo; 2.38 (s), $W_{h/2}$ 9.5 Hz, H1; 2.14, $W_{h/2}$ 10.4 Hz, H5; 1.84 (d), $^2J_{8s,8a}$ 10.9 Hz, H8s; 1.7-1.5 (m), H4exo, H6exo, H7exo, H7endo; 1.55-1.42 (m), H3exo, H3endo, H6endo; 1.38 (m), H4endo; 1.16 (m), H8a. ^{13}C nmr δ_C ($CDCl_3$) 80.2, C2; 55.8, OMe; 37.9, C1; 34.2, C5; 32.2, C8; 28.7, C4; 27.3, C7; 26.6, C6; 23.1, C3.

7-syn-Methyl-2-exo-methoxybicyclo[2.2.1]heptane (61a) (15 %): ^{1}H nmr δ_H ($CDCl_3$) 3.28 (m), $^3J_{2endo,3endo}$ 7.5 Hz, $^3J_{2endo,3exo}$ 3.2 Hz, H2endo; 3.26 (s), OMe; 2.10 (br. d), $^3J_{1,6exo}$ 3.1 Hz, H1; 1.95 (t), $^3J_{4,5exo} = {}^3J_{4,3exo}$ 3.0 Hz, H4; 1.8 - 1.65, H3exo, H3endo; 1.65 (m), H7anti; 1.55 - 1.45, H5exo, H6exo; 1.09 - 1.05, H5endo, H6endo; 1.05 (d),

$^{3}J_{CH_3,7anti}$ 7.2 Hz, CH_3. ^{13}C nmr δ_C ($CDCl_3$) 85.6, C2; 56.0, OMe; 43.6, C1, C7; 40.3, C4; 36.9, C3; 28.9, C5; 26.4, C6; 12.8, CH_3.

Preparation of 2-exo-methoxybicyclo[3.2.1]octane

The previously prepared bicyclo[3.2.1]octan-2-exo-ol (172 mg) was methylated with sodium amide methyl iodide as previously described. Isolation gave a yellow oil (124 mg, 65 %) consisting of 2-exo-methoxybicyclo[3.2.1]octane (62a) (ca. 56 %), 2-endo-methoxybicyclo[3.2.1]octane (ca. 26 %) and unreacted starting material. The ^{1}H and ^{13}C nmr data are identical with those obtained above.

Reaction of (36) with mercuric acetate in methanol and subsequent reduction

To a solution of exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) (150 mg) in anhydrous methanol (4.5 ml) was added mercuric acetate (580 mg) and the mixture stirred for 48 hours. The mixture was filtered and the solvent removed under reduced pressure. To the crude mixture was added sodium mercury amalgam (8 g, 1.5 % Na/Hg) with NaOD, D_2O (5 ml, 1M) and the reaction stirred for 3 hours. The mixture was diluted with water, the mercury decanted off and the product extracted into pentane. The combined pentane extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to yield an oil (142 mg, 73 %) shown to be a mixture of 7-syn-deutero-methyl-2-exo-methoxybicyclo[2.2.1]heptane (61b) (43 %) and 4-exo-deutero-2-exo-methoxybicyclo[3.2.1]octane (62b) (48 %). Separation was effected by preparative glc.

4-exo-Deutero-2-exo-methoxybicyclo[3.2.1]octane (62b): ^{1}H nmr δ_H ($CDCl_3$) 3.30 (s), OMe; 3.18, $W_{h/2}$ 6 Hz, H2endo; 2.38 (s),

$W_{h/2}$ 9.6 Hz, H1; 2.14 (s), $W_{h/2}$ 16.2 Hz, H5; 1.84 (d), $^{2}J_{8s,8a}$ 10.9 Hz, H8s; 1.65 (m), H6exo, H7exo, H7endo; 1.55-1.42, H3exo, H3endo, H6endo; 1.38 (d), $^{3}J_{4endo,3endo}$ 9.1 Hz, H4endo; 1.16 (m), $^{3}J_{8a,5} = {}^{3}J_{8a,1}$ 5.7 Hz, H8a. ^{2}H nmr δ_D ($CHCl_3$) 1.62, D4exo; ^{13}C nmr δ_C ($CDCl_3$) 80.4, C2; 55.8, OMe; 38.0, C1; 34.2, C5; 32.3, C8; 28.5, t, $J_{^{13}C,^{2}H}$ 18.9 Hz, C4; 27.3, C7; 26.8, C6. MS: $C_9H_{15}OD$ requires $M^{+\cdot}$ 141.1264; Found $M^{+\cdot}$ 141.1264.

7-syn-Deuteromethyl-2-exo-methoxybicyclo[2.2.1]heptane (61b): ^{1}H nmr δ_H ($CDCl_3$) 3.28 (m), $^{3}J_{2endo,3endo}$ 7.5 Hz, $^{3}J_{2endo,3exo}$ 3.2 Hz, H2endo; 3.26 (s), OMe; 2.10 (br. d), $^{3}J_{1,6exo}$ 3.1 Hz, H1; 1.95 (t), $^{3}J_{4,5exo} = {}^{3}J_{4,3exo}$ 3.0 Hz, H4; 1.8 - 1.65, H3exo, H3endo; 1.65 (t), $^{3}J_{7anti,CH_2D}$ 6.6 Hz, H7anti; 1.55 - 1.45, H5exo, H6exo; 1.09 - 1.05, H5endo, H6endo, CH_2D. ^{2}H nmr δ_D ($CHCl_3$) 1.07, CH_2D. ^{13}C nmr δ_C ($CDCl_3$) 85.7, C2; 56.2, OMe; 43.8 (L.B.), C1; 43.6 (L.B.), C7; 40.5 (L.B.), C4; 37.1, C3; 29.0, C5; 26.6, C6; 12.7, t, $J_{^{13}C,^{2}H}$ 19.1 Hz, CH_2D. (L.B.) indicates the presence of a small ^{13}C-^{2}H coupling.

Reaction of (36) with methanol-d_1, p-toluenesulphonic acid

Reaction of exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) (150 mg) with methanol-d_1 was carried out as previously described to give a pale yellow oil (174 mg, 91 %), shown to consist of 7-syn-deuteromethyl-2-exo-methoxybicyclo[2.2.1]heptane (61b) (15 %) and 4-exo-deutero-2-exo-methoxybicyclo[3.2.1]octane (62b) (76 %). Separation was effected by preparative glc. The spectral data for these compounds are identical to those obtained from the sodium mercury amalgam reduction of the products from reaction of exo-tricyclo[3.2.1.$0^{2,4}$]octane (36) with mercuric acetate, methanol above.

4-exo-deutero-2-exo-methoxybicyclo[3.2.1]octane (62b): MS shows 3 % D^0; 90 % D^1; 7 % D^2.

Reaction of (39) with mercuric acetate

To a stirred solution of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (285 mg) in anhydrous methanol (10 ml) was added mercuric acetate (950 mg). After 2 hours the mixture was filtered and the solvent removed under reduced pressure before placing under high vacuum for 12 hours to remove any acetic acid. The residue, a pale green viscous oil, was identified as (89 %) 7-exo-acetoxymercurio-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69c) (991 mg, 95 %): ^{1}H nmr δ_H ($CDCl_3$) 3.46 (d of d), $^3J_{6endo,7endo}$ 6.6 Hz, $^4J_{6endo,8s}$ 1.5 Hz, H6endo; 3.37, OMe; 2.93 (d of d), $^3J_{7endo,6endo}$ 6.6 Hz, $^4J_{7endo,8s}$ 2.9 Hz, H7endo; 2.55 (s), $W_{h/2}$ 4 Hz, H5; 2.51 (s), $W_{h/2}$ 4 Hz, H1; 2.04 (s), OAc; 1.05 (d), $^2J_{8a,8s}$ 11.1 Hz, H8a; 0.89 (d), $^2J_{8s,8a}$ 11.2 Hz, H8s; 0.77 (t of d), $^3J_{2,3endo}$ 6.8 Hz, $^3J_{2,3exo}$ 3.2 Hz, $^3J_{2,4}$ 6.8 Hz, H2; 0.68 (d of t), $^2J_{3exo,3endo}$ 6.5 Hz, $^3J_{3exo,2}$ 3.2 Hz, $^3J_{3exo,4}$ 3.2 Hz, H3exo; 0.56 (t of d), $^3J_{4,2}$ 7.0 Hz, $^3J_{4,3exo}$ 3.3 Hz, $^3J_{4,3endo}$ 6.9 Hz, H4; 0.26 (m), $^2J_{3endo,3exo}$ 6.7 Hz, $^3J_{3endo,2}$ 6.5 Hz, $^3J_{3endo,4}$ 6.5 Hz, H3endo. ^{13}C nmr δ_C, ($CDCl_3$) 176.7, OAc; 86.1, $J_{^{199}Hg,^{13}C}$ 136.3 Hz, C6; 60.1, $J_{^{199}Hg,^{13}C}$ 1761.8 Hz, C7; 56.2, OMe; 39.1, $J_{^{199}Hg,^{13}C}$ 34.4 Hz, C1; 38.6, $J_{^{199}Hg,^{13}C}$ 38.6 Hz, C5; 24.4, $J_{^{199}Hg,^{13}C}$ 16.8 Hz, C8; 22.3, OAc; 18.0, $J_{^{199}Hg,^{13}C}$ 296.2 Hz, C2; 11.2, $J_{^{199}Hg,^{13}C}$ not obs., C4; 6.2, $J_{^{199}Hg,^{13}C}$ 67.8 Hz, C3.

Reduction of (69c) with:

(a) Sodium borodeuteride.

The reduction of the organomercurial mixture (600 mg) from above was carried out as previously described to give (73:27) 7-exo- and 7-endo- deutero-6-exo-methoxy-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (119 mg, 58 %): ^{2}H nmr δ_D ($CHCl_3$) 1.71, D7endo; 1.31, D7exo.

(b) Sodium mercury amalgam.

The reduction of the organomercurial mixture (480 mg) from above was carried out as previously described to give a colourless oil (165 mg, 58 %), consisting of 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b) (89 %): ^{1}H nmr δ_H ($CDCl_3$) 3.35 (d of d), $^{3}J_{6endo,7endo}$ 7.1 Hz, $^{4}J_{6endo,8s}$ 1.4 Hz, H6endo; 3.29, OMe; 2.38 (s), $W_{h/2}$ 3 Hz, H5; 2.21 (s), $W_{h/2}$ 5 Hz, H1; 1.70 (d of t), $^{2}J_{7endo,D7exo}$ = $^{4}J_{7endo,8s}$ 2.5 Hz, $^{3}J_{7endo,6endo}$ 6.7 Hz, H7endo; 0.94 (d), $^{2}J_{8a,8s}$ 10.9 Hz, H8a; 0.83 (d of t), $^{2}J_{8s,8a}$ 11.1 Hz, $^{4}J_{8s,6endo}$ 1.8 Hz, $^{4}J_{8s,7endo}$ 1.8 Hz, H8s; 0.69 (t of d), $^{3}J_{2,3endo}$ 7.3 Hz, $^{3}J_{2,3exo}$ 3.7 Hz, $^{3}J_{2,4}$ 6.8 Hz, H2; 0.54, H3exo, H4; 0.12 (m), $^{2}J_{3endo,3exo}$ 6.4 Hz, $^{3}J_{3endo,2}$ 6.4 Hz, $^{3}J_{3endo,4}$ 6.4 Hz, H3endo. ^{2}H nmr δ_D ($CHCl_3$) 1.30, D7exo. ^{13}C nmr δ_C ($CDCl_3$) 83.9 (L.B.), C6; 56.2, OMe; 39.8, $J_{^{13}C,^{2}H}$ 19.8 Hz, C7; 39.4 (L.B.), C5; 34.8, C1; 23.4 C8; 15.9 (L.B.), C2; 11.3, C4; 4.0, C3. MS: $C_9H_{13}OD$ requires $M^{+\cdot}$ 139.1107; Found $M^{+\cdot}$ 139.1106.

Reaction of (39) with methanol, p-toluenesulphonic acid at 80°C

exo-Tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (260 mg), anhydrous methanol (4 ml) and p-toluenesulphonic acid (15 mg) were placed in an ampoule (5 ml) and kept at 80°C for 7 days. The mixture

was diluted with water (5 ml) and the product extracted into pentane. The pentane extracts were washed with aqueous sodium carbonate solution, dried over $MgSO_4$ and the solvent was removed under reduced pressure to give an oil (243 mg, 73 %), shown by glc analysis to contain 5-exo-methoxybicyclo-[2.2.2]oct-2-ene (70a) (55 %), 6-exo-methoxy-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (69a) (15 %) and some high polarity compounds of higher retention times (30 %). Separation of the volatile ethers was effected by preparative glc.

5-exo-Methoxybicyclo[2.2.2]oct-2-ene (70a): ^{1}H nmr δ_H ($CDCl_3$) 6.29 (t), $^3J_{2,3}$ 7.7 Hz, $^3J_{2,1}$ 7.7 Hz, H2; 6.15 (t of d), $^3J_{3,2} = {}^3J_{3,4}$ 7.5 Hz, $^4J_{3,1}$ 1.8 Hz, H3; 3.30, OMe, H5endo; 2.76 (s), $W_{h/2}$ 11 Hz, H4; 2.49 (s), $W_{h/2}$ 13 Hz, H1; 1.90 (m), $^2J_{8s,8a}$ 12.7 Hz, $^3J_{8s,4}$ 2.3 Hz, $^3J_{8s,7a}$ 2.3 Hz, $^3J_{8s,7s}$ 8.1 Hz, H8s; 1.73 (m), $^2J_{6endo,6exo}$ 13.2 Hz, $^3J_{6endo,1}$ 3.4 Hz, $^3J_{6endo,5endo}$ 9.7 Hz, $^3J_{6endo,7a}$ 3.4 Hz, H6endo; 1.60 (m), $^2J_{7s,7a}$ 11.8 Hz, $^3J_{7s,1}$ 2.6 Hz, $^3J_{7s,8a}$ 3.9 Hz, $^3J_{7s,8s}$ 9.0 Hz, H7s; 1.25 (m), $^2J_{7a,7s} = {}^3J_{7a,8a}$ 12.0 Hz, $^3J_{7a,1}$ 3.1 Hz, $^3J_{7a,8s}$ 4.4 Hz, H7a; 1.17 (d of t), $^2J_{6exo,6endo}$ 13.2 Hz, $^3J_{6exo,1}$ 2.5 Hz, $^3J_{6exo,5endo}$ 2.5 Hz, H6exo; 1.05 (m), $^2J_{8a,8s}$ 12.3 Hz, $^3J_{8a,4}$ 2.8 Hz, $^3J_{8a,7a}$ 12.3 Hz, $^3J_{8a,7s}$ 4.4 Hz, $^4J_{8a,5endo}$ 1.7 Hz, H8a. ^{13}C nmr δ_C ($CDCl_3$) 136.1, C2; 131.4, C3; 78.5, C5; 56.0, OMe; 33.5, C6; 33.2, C4; 29.8, C1; 25.9, C7; 17.6, C8. MS: $C_9H_{14}O$ requires $M^{+\cdot}$ 138.1045. Found $M^{+\cdot}$ 138.1043.

6-exo-Methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69a): ^{1}H nmr δ_H ($CDCl_3$) 3.35 (d of t), $^3J_{6endo,7endo}$ 6.6 Hz, $^3J_{6endo,7exo}$ 1.8 Hz, $^4J_{6endo,8s}$ 1.8 Hz, H6endo; 3.29, OMe; 2.38 (s), $W_{h/2}$ 4 Hz, H5; 2.21 (s), $W_{h/2}$ 7 Hz, H1; 1.73 (m), $^2J_{7endo,7exo}$ 12.3 Hz, $^3J_{7endo,6endo}$ 6.8 Hz, $^4J_{7endo,8s}$ 2.6 Hz, H7endo; 1.31 (d of t), $^2J_{7exo,7endo}$ 12.4 Hz, $^3J_{7exo,1}$ 3.1

Hz, $^{3}J_{7\underline{exo},6\underline{endo}}$ 3.1 Hz, H7exo; 0.95 (d), $^{2}J_{8a,8s}$ 11.0 Hz, H8a; 0.84 (d of t), $^{2}J_{8s,8a}$ 11.0 Hz, $^{4}J_{8s,6\underline{endo}}$ 2.1 Hz, $^{4}J_{8s,7\underline{endo}}$ 2.1 Hz, H8s; 0.70 (t of d), $^{3}J_{2,3\underline{endo}}$ 7.3 Hz, $^{3}J_{2,3\underline{exo}}$ 3.6 Hz, $^{3}J_{2,4}$ 7.3 Hz, H2; 0.54 (m), H3exo, H4; 0.12 (m), $^{2}J_{3\underline{endo},3\underline{exo}}$ 6.4 Hz, $^{3}J_{3\underline{endo},2}$ 6.4 Hz, $^{3}J_{3\underline{endo},4}$ 6.4 Hz, H3endo. ^{13}C nmr δ_C ($CDCl_3$) 84.0, C6; 56.3, OMe; 40.2, C7; 39.5, C5; 34.9, C1; 23.5. C8; 16.0, C2; 11.3, C4; 4.1, C3. MS: $C_9H_{14}O$ requires $M^{+\cdot}$ 138.1045; Found $M^{+\cdot}$ 138.1045.

Reaction of (39) with methanol-d_1, p-toluenesulphonic acid at 80°C

The acid catalysed reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (273 mg) with methanol-d_1 at 80°C for 7 days was carried out as previously described. Isolation gave (56:12) 7-syn-deutero-5-exo-methoxybicyclo[2.2.2]oct-2-ene (70b) and 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b) (304 mg, 87 %). Separation was achieved by careful preparative glc.

7-syn-Deutero-5-exo-methoxybicyclo[2.2.2]oct-2-ene (70b): ^{1}H nmr δ_H ($CDCl_3$) 6.29 (t), $^{3}J_{2,3}$ 7.7 Hz, $^{3}J_{2,1}$ 7.7 Hz, H2; 6.15 (t of d), $^{3}J_{3,2} = {}^{3}J_{3,4}$ 7.5 Hz, $^{4}J_{3,1}$ 1.3 Hz, H3; 3.30, OMe, H5endo; 2.76 (s), $W_{h/2}$ 12 Hz, H4; 2.49 (s), $W_{h/2}$ 11 Hz, H1; 1.90 (m), $^{2}J_{8s,8a}$ 12.3 Hz, $^{3}J_{8s,4}$ 2.3 Hz, $^{3}J_{8s,7a}$ 2.3 Hz, (broadened due to its proximity to ^{2}H-7s), H8s; 1.73 (m), $^{2}J_{6\underline{endo},6\underline{exo}}$ 13.2 Hz, $^{3}J_{6\underline{endo},1}$ 3.4 Hz, $^{3}J_{6\underline{endo},5\underline{endo}}$ 9.7 Hz, $^{3}J_{6\underline{endo},7a}$ 3.4 Hz, H6endo; 1.23, H7a; 1.17 (d of t), $^{2}J_{6\underline{exo},6\underline{endo}}$ 13.1 Hz, $^{3}J_{6\underline{exo},1}$ 2.2 Hz, $^{3}J_{6\underline{exo},5\underline{endo}}$ 3.3 Hz, H6exo; 1.05 (m), $^{2}J_{8a,8s}$ 12.2 Hz, $^{3}J_{8a,4}$ 3.1 Hz, $^{3}J_{8a,7a}$ 12.2 Hz, $^{4}J_{8a,5\underline{endo}}$ 1.6 Hz, H8a. ^{2}H nmr δ_D ($CDCl_3$) 1.60, D7s. ^{13}C nmr δ_C ($CDCl_3$) 136.1 (L.B.), C2; 131.5, C3;

78.5, C5; 56.2, OMe; 33.5, C6; 33.2, C4; 29.7 (L.B.), C1; 25.5, $J_{^{13}C,^{2}H}$ 19.7 Hz, C7; 17.5, C8. MS: $C_9H_{13}OD$ requires $M^{+\cdot}$ 139.1107; Found $M^{+\cdot}$ 139.1103. Mass spectrum shows 7 % D^0, 77 % D^1, 16 % D^2.

7-exo-Deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b): All spectral data are identical with those reported in the sodium mercury amalgam reduction in NaOD, D_2O of 7-exo-acetoxymercurio-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]-octane (69c).

Reaction of (39) with methanol, p-toluenesulphonic acid at room temperature

To exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (1.156 g) was added anhydrous methanol (10 ml) and p-toluenesulphonic acid (384 mg). The mixture was stirred for 28 days (77 % reaction), diluted with water and the product extracted into pentane. The combined pentane extracts were washed with aqueous sodium bicarbonate solution, dried over $MgSO_4$ and the solvent removed under reduced pressure to give a pale yellow oil (1.035 g, 80 %), consisting of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (23 %), 5-exo-methoxybicyclo[2.2.2]oct-2-ene (70a) (23 %), 6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69a) (18 %) and 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71a) (31 %), in addition to two unidentified compounds (2 % and 3 %). 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71a) was isolated by preparative glc: ^{1}H nmr δ_H ($CDCl_3$) 3.52 (s), $W_{h/2}$ 2.0 Hz, H6endo; 3.34 (s), OMe; 1.96 (br. s), $W_{h/2}$ 11.4 Hz, H5; 1.88 (m), $^2J_{8a,8s}$ 11.4 Hz, $^3J_{8a,1}$ 3.4 Hz, $^3J_{8a,5}$ 5.7 Hz, $^4J_{8a,4endo}$ 2.2 Hz, H8a; 1.78 - 1.68 (m), H3exo, H3endo; 1.58, H4exo; 1.51, H7, H8s; 1.40, H1; 1.32, H4endo; 0.92 (m), $^3J_{2,1}$ 8.0 Hz, $^3J_{2,3exo} = {}^3J_{2,3endo}$ 2.7 Hz, $^3J_{2,7}$ 8.0 Hz, H2.

^{13}C nmr δ_C ($CDCl_3$) 85.5, C6; 55.7, OMe; 34.9, C5; 27.4, C8; 26.5, C4; 22.0, C7; 16.9, C1; 16.5, C2; 16.1, C3.

The spectral data for 5-exo-methoxybicyclo[2.2.2]oct-2-ene (70a) and 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (69a) are identical with those reported in the acid catalysed methanol addition at 80°C.

Reaction of (39) with methanol-d_1, p-toluenesulphonic acid at room temperature

To exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (55 mg) was added a solution of p-toluenesulphonic acid (25 mg) in methanol-d_1 (2 ml). The mixture was stirred for 72 days (75 % reaction) to give 7-syn-deutero-5-exo-methoxybicyclo[2.2.2]oct-2-ene (70b) (28 %), 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (69b) (16 %) and 4-exo-deutero-6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71b) (31 %). 4-exo-Deutero-6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71b): ^{13}C nmr δ_C ($CDCl_3$) 85.5, C6; 55.7, OMe; 34.7, C5; 27.4, C8; 26.1, $J_{^{13}C,^{2}H}$ 19.9 Hz, C4; 22.0, C7; 16.9, C1; 16.5, C2; 16.2, C3. ^{2}H nmr δ_D ($CHCl_3$) 1.52, D4exo.

Stability of (69b) and (71a) under the reaction conditions

(i) 7-exo-Deutero-6-exo-methoxytricyclo[3.2.1.$0^{2,4}$]octane (69b): To an ampoule containing 7-exo-deutero-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (45 mg, prepared from the sodium mercury amalgam reduction of the organomercurial (69c) in NaOD) was added 0.7 ml of a solution of p-toluenesulphonic acid (21 mg) in methanol (10 ml). The ampoule was sealed and placed in an oven at 80°C for 7 days, after which time glc analysis revealed the presence of 7-exo-deutero-6-exo-methoxy-exo-

tricyclo[3.2.1.$0^{2,4}$]octane (69b) (52 %), high retention time compounds (35 %) and three other compounds (2 %, 8 % and 2 %). (ii) 6-exo-Methoxytricyclo[3.2.1.$0^{2,7}$]octane (71a): To a flask containing 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (5 mg; obtained by preparative glc from the products of the acid catalysed reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene with methanol at 25°C), was added 0.6 ml of a solution of p-toluenesulphonic acid (215 mg) in methanol (10 ml). The contents of the flask were stirred and monitored by glc. Approximately 2 hours after the start of the reaction, glc revealed the mixture to contain 5-exo-methoxybicyclo-[2.2.2]oct-2-ene (70a) (45 %) and 6-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (71a) (55 %). This product ratio was invariant for 16 days.

Reaction of (35) with methanol, p-toluenesulphonic acid at room temperature

To a flask containing 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]-octane (35) (118 mg) was added 2 ml of a solution containing p-toluenesulphonic acid (181 mg) in methanol (10 ml). The mixture was stirred at room temperature for 4 days, diluted with water (5 ml) and the product extracted into pentane. The pentane extracts were washed with aqueous sodium carbonate solution, dried over $MgSO_4$, and the solvent removed under reduced pressure to yield a colourless oil (103 mg, 75 %) shown to contain 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (19 %), 2-methylbicyclo[3.2.1]oct-2-ene (74a) (18 %), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) (32 %) and 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) (31 %). Separation was achieved by preparative glc.

2-Methylbicyclo[3.2.1]oct-2-ene (74a): ^{1}H nmr δ_H ($CDCl_3$) 5.03 (br s), $W_{h/2}$ 8 Hz, H3; 2.27, $W_{h/2}$ 16 Hz, H4exo, H5; 2.12 (t), $^{3}J_{1,8a} = {}^{3}J_{1,7exo}$ 4.2 Hz, H1; 1.8 - 1.3 (m), 10 H. The following assignments were determined from a heteronuclear correlation experiment: 1.76, H6exo; 1.73, H4endo; 1.70, H7exo, H7endo; 1.65, Me; 1.50, H8s, H8a; 1.40, H6endo. ^{13}C nmr δ_C ($CDCl_3$) 141.9, C2; 116.6, C3; 40.7, C1; 36.8, C4; 35.3, C8; 34.5, C7; 33.2, C5; 30.5, C6; 21.9, Me.

2-endo-Methoxy-2-exo-methylbicyclo[3.2.1]octane (72a): ^{1}H nmr δ_H ($CDCl_3$) 3.17 (s), OMe; 2.13, $W_{h/2}$ 11 Hz, H1, H5; 1.84 (m), H7exo; 1.68 - 1.55 (m, 2H), H8a, H6exo; 1.5 - 1.3 (m, 7H's), H8s, H4exo, H4endo, H3exo, H3endo, H7endo, H6endo; 1.20 (s), Me. The following assignments were determined from a heteronuclear correlation experiment: 1.65, H6exo; 1.56, H8a; 1.51, H7endo; 1.55 - 1.45, H3exo, H3endo; 1.43, H4exo, H4endo, H6endo; 1.28, H8s. ^{13}C nmr δ_C ($CDCl_3$) 76.8, C2; 48.0, OMe; 42.9, C1; 35.5, C8; 34.5, C5; 31.4, C3; 30.0, C4; 27.6, C6; 24.5, C7; 20.9, Me.

2-exo-Methoxy-2-endo-methylbicyclo[3.2.1]octane (73a): ^{1}H nmr δ_H ($CDCl_3$) 3.18, OMe; 2.10, $W_{h/2}$ 15 Hz, H5, H1; 1.94 (d of t), $^{2}J_{8s,8a}$ 11 Hz, $^{4}J_{8s,6endo} = {}^{4}J_{8s,7endo}$ 1.5 Hz, H8s; 1.7 - 1.55 (m, 3H's), H4exo, H7exo, H6exo; 1.50 - 1.35 (m, 3H's), H6endo, H3exo, H7endo; 1.30 - 1.15 (m, 3H's), H4endo, H3endo, H8a; 1.06 (s), Me. The following assignments were determined from a heteronuclear correlation experiment: 1.73, H6exo, H7exo; 1.65, H4exo; 1.50 - 1.26, H3exo, H3endo; 1.42, H6endo, H7endo; 1.26, H4endo; 1.19, H8a. ^{13}C nmr δ_C ($CDCl_3$) 77.2, C2; 48.5, OMe; 43.4, C1; 33.6, C5; 33.3, C8; 29.7, C3; 29.0, C4; 28.0, C6; 26.8, C7; 22.3, Me.

Preparation of (77b) and (78b)

3,3,4-exo-Trideuterobicyclo[3.2.1]octan-2-one (46) (370 mg), as prepared earlier, was reacted with MeMgI[96] (prepared from 300 mg magnesium and 0.6 ml CH_3I) in ether to give a mixture of 2-exo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-endo-ol (77a) and 2-endo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-exo-ol (78a) (272 mg, 65 %; 66:34) as a white solid.

2-exo-Methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-endo-ol (77a): ^{13}C nmr δ_C ($CDCl_3$) 72.8, C2; 47.6, C1; 35.9, C8; 33.8, C5; 29.6, triplet, $J_{^{13}C,^{2}H}$ 19.4 Hz, C4; 27.5, Me; 26.9, C6; 24.9, C7. Note: the ^{13}C nmr is revised from reference 64.

2-endo-Methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-exo-ol (78a): ^{13}C nmr δ_C ($CDCl_3$) 72.9, C2; 46.8, C1; 33.4, C5; 29.0, C6, C8; 28.3, t, $J_{^{13}C,^{2}H}$ 19.0 Hz, C4; 27.1, Me; 24.9, C7; C3, not obs.

The mixture (100 mg), was methylated with sodium amide methyl iodide as described earlier to give a mixture of 2-exo-methoxy-2-endo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octane (78b) and 2-endo-methoxy-2-exo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octane (77b) as an oil (75 mg, 70 %). The spectral analysis is obtained from the mixture of epimers.

2-endo-Methoxy-2-exo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octane (77b): ^{13}C nmr δ_C ($CDCl_3$) 76.5, C2; 47.9, OMe; 42.8, C1; 35.4, C8; 34.3, C5; 29.4, triplet, $J_{^{13}C,^{2}H}$ 19.0 Hz, C4; 27.5, C6; 24.4, C7; 20.7, Me; C3, not observed.

2-exo-Methoxy-2-endo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octane (78b): ^{13}C nmr δ_C ($CDCl_3$) 76.7, C2; 48.3, OMe; 43.3, C1; 33.4, C5; 33.2, C8; 28.3, triplet, $J_{^{13}C,^{2}H}$ 19.0 Hz, C4; 27.9, C6; 26.7, C7; 22.2, Me; C3, not observed.

Preparation of deutero-2-methylbicyclo[3.2.1]oct-2-ene

A mixture of 2-endo-methyl-3,3,4-exo-trideuterobicyclo-[3.2.1]octan-2-exo-ol (78a) and 2-exo-methyl-3,3,4-exo-trideuterobicyclo[3.2.1]octan-2-endo-ol (77a) (260 mg, obtained from the reaction of 3,3,4-exo-trideuterobicyclo[3.2.1]-octan-2-one (46) with MeMgI) was stirred under reflux with $KHSO_4$ (200 mg) at 160°C for 30 minutes. The mixture was allowed to cool and after addition of water (5 ml) and ether (5 ml) the two layers were separated and the aqueous layer extracted with ether. The combined ether extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure to give 2-methyl-3,4-exo-dideuterobicyclo[3.2.1]oct-2-ene (200 mg, 85%). ^{13}C nmr δ_C ($CDCl_3$) 116.5, C3; 48.4, C1; 36.5, $J_{^{13}C,^{2}H}$ 18.1 Hz, C4; 35.3, C8; 34.4, C7; 32.7, C5; 30.5, C6; 22.5, Me. ^{2}H nmr δ_D ($CHCl_3$) 5.05 (0.25 D), D3; 2.30 (0.53 D), D4exo; 1.75 (0.29 D), D4endo; 1.65 (0.40 D), Me.

Stability of (72a) and (73a) at room temperature under the reaction conditions

(i) 2-endo-Methoxy-2-exo-methylbicyclo[3.2.1]octane (72a): To a flask containing 2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (85 mg, prepared from the $NaBH_4$ reduction of 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (72c)) was added 1.3 ml of a solution containing p-toluenesulphonic acid (493 mg) in anhydrous methanol (25 ml). The flask was stoppered and the contents stirred. A sample was taken for glc analysis every few days and the epimer ratio was shown to be invariant for 21 days.

(ii) 2-exo-Methoxy-2-endo-methylbicyclo[3.2.1]octane (73b): To a flask containing 4-endo-deutero-2-exo-methoxy-2-endo-methyl-

bicyclo[3.2.1]octane (16 mg, obtained by preparative glc of the reaction mixture of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with methanol-d_1 at room temperature, and contaminated with 32 % of 4-endo-deutero-2-endo-methoxy-2-exo-methylbicylo-[3.2.1]octane (72b)) was added 1.0 ml of a solution containing p-toluenesulphonic acid (493 mg) in anhydrous methanol (25 ml). The flask was stoppered and the contents stirred. A sample was taken for glc analysis every few days and the ratio of epimers shown to be invariant for 21 days.

Reaction of (35) with mercuric acetate

To a solution of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (120 mg) in anhydrous methanol (1 ml) was added, with stirring, mercuric acetate (320 mg) and the mixture stirred for 4 hours. The mixture was filtered to remove any unreacted mercuric acetate, the solvent removed under reduced pressure and the mixture placed under high vacuum for 12 hours to remove acetic acid and give (9:1) 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72c) and 4-endo-acetoxymercurio-2-exo-methoxy-2-endo-methyl-bicyclo[3.2.1]octane (73c) (310 mg, 82 %) as a white solid. 4-endo-Acetoxymercurio-2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]octane (72c): ^{1}H nmr δ_H ($CDCl_3$) 3.16, OMe; 2.83 (m), $^3J_{4exo,3endo}$ 13.6 Hz, $^3J_{4exo,3exo}$ 5.2 Hz, $^3J_{4exo,5}$ = $^4J_{4exo,6exo}$ 1.5 Hz, H4exo; 2.49, $^3J_{5,6exo}$ = $^3J_{5,8a}$ 5.1 Hz, $J_{^{199}Hg,H5}$ 120 Hz, H5; 2.07 (m), H1; 2.02 (s), OAc; 1.98 (m), H7exo; 1.90-1.78 (m), H3exo, H3endo, H6exo; 1.60-1.45 (m), H8a, H8s, H6endo, H7endo; 1.20 (s), Me. The following assignments were determined from a heteronuclear correlation experiment: 1.92, H3exo; 1.85, H3endo; 1.79, H6exo; 1.56, H8s; 1.52, H8a; 1.48, H7endo; 1.45, H6endo. ^{13}C nmr δ_C ($CDCl_3$) 176.1, OAc;

76.9, $J_{^{199}Hg-^{13}C}$ ca. 284 Hz, C2; 51.7, $J_{^{199}Hg-^{13}C}$ 1662 Hz, C4; 48.0, OMe; 43.2, $J_{^{199}Hg-^{13}C}$ 27 Hz, C1; 40.5, $J_{^{199}Hg-^{13}C}$ 74 Hz, C5; 38.1, $J_{^{199}Hg-^{13}C}$ 67 Hz, C3; 36.8, $J_{^{199}Hg-^{13}C}$ 255 Hz, C8; 30.2, $J_{^{199}Hg-^{13}C}$ 28 Hz, C6; 24.2, no $^{199}Hg-^{13}C$ coupling observed, C7; 23.4, OAc; 20.5, Me.

Elemental analysis: $C_{12}H_{20}O_3Hg$ requires 34.91 % C, 4.88 % H; Found 34.89 % C; 4.91 % H.

A solution of the organomercurial mixture above (300 mg), dissolved in the minimum amount of methanol, was shaken with a saturated solution of potassium thiocyanate in water (2 ml). The mixture was extracted with chloroform, dried over $MgSO_4$ and the solvent removed under reduced pressure to give an oil (285 mg, 95 %), consisting mainly of 2-endo-methoxy-2-exo-methyl-4-endo-thiocyanatomercuriobicyclo[3.2.1]octane (72d), ^1H nmr δ_H ($CDCl_3$) 3.18 (s), OMe; 2.91 (m), $^3J_{4exo,3endo}$ 13.7 Hz, $^3J_{4exo,3exo}$ 5.2 Hz, $^3J_{4exo,5} = {}^4J_{4exo,6exo}$ 1.6 Hz, H4exo; 2.57 (br. s), $W_{h/2}$ 13.4 Hz, H5; 2.14 - 1.80 (m), H1, H7exo, H3exo, H3endo, H6exo; 1.60 - 1.50 (m), H7endo, H8s, H8a, H6endo; 1.23 (s), Me. The following assignments were determined from a heteronuclear correlation experiment: 2.10, H1; 1.99, H7exo, ca. 1.96, H3exo, H3endo; 1.88, H6exo; 1.54, H7endo, H8s, H8a; 1.53, H6endo. ^{13}C nmr δ_C ($CDCl_3$) 61.9, C4; 48.1, OMe; 43.0, C5; 41.0, C1; 38.2, C3; 37.2, C8; 30.5, C6; 24.3, C7; 20.6, Me; C2, not obs.

Reduction of (72c) with sodium mercury amalgam

The reduction of the organomercurial mixture from above (106 mg) was carried out as described in the reduction of 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]octane (40c) and gave a colourless oil (27 mg, 68 %) shown to consist of

4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b) (93 %) and 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b) (7 %). Separation of the major product was achieved by preparative glc.

4-endo-Deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b): ^{1}H nmr δ_H ($CDCl_3$) 3.17 (s), OMe; 2.13, $W_{h/2}$ 16 Hz, H1, H5; 1.84 (m), H7exo; 1.68 - 1.55 (m, 2H), H8 ,H6exo; 1.5 - 1.3 (m, 6H),H8 , H4exo, H4endo, H3exo, H3endo, H7endo, H6endo; 1.20 (s), Me. The spectrum was almost identical with that of the non deuterated compound. ^{13}C nmr δ_C ($CDCl_3$) 76.8, C2; 48.0, OMe; 43.0, C1; 35.5 (L.B.), C8; 34.4, C5; 31.4, C3; 29.7, $J_{^{13}C,^{2}H}$ 19.6 Hz, C4; 27.7, C6; 24.6, C7; 21.0, Me. ^{2}H nmr δ_D ($CHCl_3$) 1.41, D4endo.

Reaction of (35) with methanol, p-toluenesulphonic acid at 80°C

2-Methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (240 mg), anhydrous methanol (2 ml) and p-toluenesulphonic acid (9 mg) were placed in an ampoule (5 ml) and kept at 80°C for 7 days. The mixture was diluted with water (5 ml) and the product extracted into pentane. The pentane extracts were washed with aqueous sodium carbonate solution, dried over $MgSO_4$ and the solvent removed under reduced pressure to give a light yellow oil (247 mg, 82%), shown to contain 2-methylbicyclo[3.2.1]-oct-2-ene (74a) (53%), 2-methoxy-1-methylbicyclo[2.2.2]octane (81a) (8%), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) (21%), and 2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (74a) (18%). Separation was achieved by preparative glc.

2-exo-Methoxy-1-methylbicyclo[2.2.2]octane (81a): ^{1}H nmr δ_H ($CDCl_3$) 3.32 (s), OMe; 3.02 (m), $^{3}J_{2endo,3endo}$ 9.0 Hz,

$^{3}J_{2\underline{endo},3\underline{exo}}$ 3.5 Hz, $^{3}J_{2\underline{endo},6a}$ 1.7 Hz, H2endo; 1.84 (m), $^{2}J_{3\underline{endo},3\underline{exo}}$ 12.4 Hz, $^{4}J_{3\underline{endo},2\underline{endo}}$ 8.6 Hz, $^{3}J_{3\underline{endo},4}$ = $^{4}J_{3\underline{endo},5a}$ 2.9 Hz, H3endo; 1.64 (m), H4, H6s; 1.55 - 1.38 (m, 6H's), H5s, H3exo, H5a, H7exo, H8exo, H8endo; 1.28 (m), $^{2}J_{7\underline{endo},7\underline{exo}}$ 12 Hz, $^{3}J_{7\underline{endo},8\underline{endo}}$ 7.8 Hz, $^{3}J_{7\underline{endo},8\underline{exo}}$ 3.6 Hz, $^{4}J_{7\underline{endo},6s}$ 1.2 Hz, H7endo; 1.08 (m), H6a; 0.83 (s), Me. The following assignments were determined from a heteronuclear correlation experiment: 1.54, H5s; 1.51, H8exo; 1.49, H3exo; 1.46, H5a; 1.43, H7exo; 1.41, H8endo. ^{13}C nmr δ_C ($CDCl_3$) 82.8, C2; 56.3, OMe; 34.5, C3; 32.1, C7; 26.2, C6; 26.0, C5; 25.6, C8; 24.8, C4; 24.7, Me; Cl not observed. MS: $C_{10}H_{18}O$ requires $M^{+\cdot}$ 154.1358; Found $M^{+\cdot}$ 154.1354. 155 (9 %), 154 (25 %), 123 (19 %), 122 (51 %), 107 (13 %), 95 (23 %), 94 (100 %), 93 (36 %), 81 (47 %), 79 (30 %). The spectral data for 2-methylbicyclo[3.2.1]oct-2-ene (74a), 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) and 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) are identical to those reported for the compounds isolated from the acid catalysed methanol addition at room temperature.

Stability of (72a), (73a) and (74a) under the reaction conditions at 80°C

(i) 2-endo-Methoxy-2-exo-methylbicyclo[3.2.1]octane (72a): To an ampoule containing 2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (85 mg, prepared from the $NaBH_4$ reduction of 4-endo-acetoxymercurio-2-endo-methoxy-2-exo-methylbicyclo-[3.2.1]octane (72c)) was added 0.7 ml of a solution containing p-toluenesulphonic acid (493 mg) in methanol (25 ml) and the ampoule sealed and placed in an oven at 80 degrees. At the end of eight days a sample was removed for glc analysis which showed a mixture of 2-methylbicyclo[3.2.1]oct-2-ene (74a),

2-exo-methoxy-1-methylbicyclo[2.2.2]octane (81a), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) and 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) in the ratio of 67:16:9:8 respectively. After the product was isolated, ^{1}H and ^{13}C nmr analysis confirmed the above results. In a separate experiment, but after 26 hours, the product was a mixture (92:0:4:2) of (74a), (81a), (72a) and (73a) respectively.

(ii) 2-exo-Methoxy-2-endo-methylbicyclo[3.2.1]octane (73a): 2-exo-Methoxy-2-endo-methylbicyclo[3.2.1]octane (16 mg, obtained from preparative glc of the products from the acid catalysed reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with methanol and contaminated with 32 % of 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a)) was kept at 80°C under the above conditions to give, after 8 days, a mixture of 2-methylbicyclo[3.2.1]oct-2-ene (74a), 2-methoxy-1-methylbicyclo[2.2.2]octane (81a), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) and 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) in the ratio of 69:16:8:8 respectively.

(iii) 2-Methylbicyclo[3.2.1]oct-2-ene (74a): 2-Methylbicyclo-[3.2.1]oct-2-ene (22 mg, obtained by preparative glc from the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) and methanol at 80°) was added to an ampoule containing anhydrous methanol (3 ml) and p-toluenesulphonic acid (5 mg). The ampoule was sealed and placed in an oven at 80° for 7 days. Subsequent glc analysis revealed the presence of 2-exo-methoxy-1-methylbicyclo[2.2.2]octane (81a), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a), 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) and 2-methylbicyclo[3.2.1]oct-2-ene (74a) in the ratio 2:34:36:28

respectively. Isolation of the product and analysis of the ^{1}H and ^{13}C nmr spectra confirmed the above results.

Reaction of (35) with methanol-d_1, p-toluenesulphonic acid at room temperature

The reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (268 mg) with methanol-d_1 was carried out as previously described for the room temperature reaction with methanol. The product was isolated after 7 days to give a colourless oil (230 mg, 68 %) shown to contain 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]-octane (35) (26 %), 4-endo-deutero-2-methylbicyclo[3.2.1]-oct-2-ene (74b) (16 %), 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b) (30 %) and 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b) (28 %). Separation was achieved by preparative glc. 4-endo-Deutero-2-methylbicyclo[3.2.1]oct-2-ene (74b): ^{1}H nmr δ_H ($CDCl_3$) 5.03 (br s), $W_{h/2}$ 8 Hz, H3; 2.27, $W_{h/2}$ 16 Hz, H4exo, H5; 2.12 (t), $^{3}J_{1,8a} = {}^{3}J_{1,7exo}$ 4.2 Hz, H1; 1.8 - 1.3 (m), 9 H's. The spectrum was almost identical to that of the non deuterated compound. ^{13}C nmr δ_C ($CDCl_3$) 141.9, C2; 116.3, C3; 40.4, C1; 36.3, $J_{^{13}C,^{2}H}$ 19.8 Hz, C4; 34.7 (L.B.), C8; 34.5, C7; 33.0 (L.B.), C5; 30.5, C6; 21.8, Me. ^{2}H nmr δ_D ($CHCl_3$) 1.75, D4endo.

4-endo-Deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b): ^{1}H nmr δ_H ($CDCl_3$) 3.18, OMe; 2.10, $W_{h/2}$ 11.8 Hz, H5, H1; 1.94, $^{2}J_{8s,8a}$ 11 Hz, $^{4}J_{8s,6endo} = {}^{4}J_{8s,7endo}$ 1.5 Hz, H8s; 1.7 - 1.55 (m, 3H's), H4exo, H7exo, H6exo; 1.50 - 1.35 (m, 3H's), H6endo, H3exo, H7endo; 1.30 - 1.15 (m, 2H's), H3endo, H8a; 1.06 (s), Me. The spectrum was almost identical to that of the non deuterated compound. ^{13}C nmr δ_C ($CDCl_3$) 77.2, C2; 48.5, OMe; 43.4, C1; 33.5 (L.B.), C5; 33.3 (L.B.), C8; 29.6,

C3; 28.6, $J_{^{13}C,^{2}H}$ 19.8 Hz, C4; 28.0, C6; 26.9, C7; 22.4, Me. ^{2}H nmr δ_D ($CHCl_3$) 1.23, D4endo.

The spectral data for 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b) are identical to those reported in the major product from the sodium mercury reduction of the organomercurial mixture above. The C4-endo-H and C4-exo-H both absorb at 1.42 ppm in the non deuterated compound.

A study of the spectrum of a mixture of 4-exo- and 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane, obtained from the sodium borodeuteride reduction of the reaction products from the reaction of 2-endo-methyl-tricyclo[3.2.1.$0^{2,4}$]octane with mercuric acetate in methanol (carried out as outlined in the reduction of 4-endo-acetoxymercurio-2-endo-methoxybicyclo[3.2.1]octane (40c)), with $Eu(fod)_3$ was carried out. To a $CHCl_3$ solution of 8.6 mg of the reduction products was added, incrementally, a total of 78 mg of $Eu(fod)_3$, and the ^{2}H nmr run (with heteronuclear proton-deuteron decoupling). No resolution of the 4exo- and 4endo- deuterons was obtained.

The following epimerisation was undertaken. To an ampoule (1 ml) containing 4-deutero-2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]octane (72b) (26 mg, obtained by preparative glc of the products of the reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with methanol-d_1 at room temperature and contaminated with 24 % 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b)) was added 0.7 ml of a solution containing p-toluenesulphonic acid (54 mg) in methanol (5 ml). The ampoule was sealed and placed in an oven at 80° for 32 hours. The product was isolated in the usual manner and glc, ^{1}H and

^{13}C nmr confirmed the presence of 4-deutero-2-methylbicyclo[3.2.1]oct-2-ene (57 %), 4-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (23 %) and 4-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]-octane (19 %). ^{2}H nmr δ_D ($CDCl_3$) 1.75, 4-endo-deutero-2-methylbicyclo[3.2.1]oct-3-ene (74b); 1.41, 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72b); 1.24, 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73b).

Reaction of (35) with methanol-d_1, p-toluenesulphonic acid at 80°C

The reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) (240 mg) with methanol-d_1, p-toluenesulphonic acid was carried out as above, but at 80°C for 7 days. The product was isolated as a light yellow oil (247 mg, 82 %) and shown by glc analysis to contain 4 compounds (42 %, 21 %, 19 %, 17 %). The products were separated by preparative glc.

3,4-endo,9,9-tetra-Deutero-2-methylbicyclo[3.2.1]oct-2-ene (74) (42 %): ^{1}H nmr δ_H ($CDCl_3$) essentially as reported above, except 5.01 ppm (0.13 H), H3. ^{13}C nmr δ_C ($CDCl_3$) 40.4, C1; 36.5, $J_{^{13}C,^{2}H}$ 18.9 Hz, C4; 35.3, C8; 34.5, C7; 32.7, C5; 30.5, C6; C2, C3, Me not observed. ^{2}H nmr δ_D ($CHCl_3$) 5.08 (0.82 D), D3; 1.78, (0.98 D), D4endo; 1.62, (2.46 D), Me. Mass spectrum shows 1 % D^0, 7 % D^1, 14 % D^2, 10 % D^3, 30 % D^4, 38 % D^5.

3,3,4-endo,9,9-penta-Deutero-2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]octane (72) (17 %): ^{1}H nmr δ_H ($CDCl_3$) essentially as reported above, except 1.18 (m) (0.68 H), Me. ^{13}C nmr δ_C ($CDCl_3$) 76.8, C2; 48.0, OMe; 42.9, C1; 35.4, C8; 34.3, C5; 27.6, C6; 24.5, C7; C3, C4, Me not observed. ^{2}H nmr δ_D ($CHCl_3$) 1.42 (2.43 D), D4endo, D3exo, D3endo; 1.18 (2.20 D),

Me. Mass spectrum shows 1 % D^0, 10 % D^1, 1 % D^2, 4 % D^3, 16 % D^4, 35 % D^5, 33 % D^6.

3,3,4-endo,9,9-penta-Deutero-2-exo-methoxy-2-endo-methyl-bicyclo[3.2.1]octane (73) (19 %): ^1H nmr δ_H ($CDCl_3$) is almost identical with that observed for the non deuterated compound except the loss of H4endo reveals 1.18, $^2J_{8a,8s}$ 11.0 Hz, $^3J_{8a,1} = {}^3J_{8a,5}$ 5.4 Hz, H8a; 1.02 (m) (0.35 H), Me. ^{13}C nmr δ_C ($CDCl_3$) 77.2, C2; 48.5, OMe; 43.3, C1; 33.5, C5; 33.2, C8; 27.9, C6; 26.8, C7; C3, C4, Me not observed. ^2H nmr δ_D ($CHCl_3$) 1.42, D3exo; 1.23, D4endo; 1.18, D3endo; 1.04 (2.57 D), Me. Mass spectrum shows 6 % D^0, 5 % D^3, 16 % D^4, 35 % D^5, 35 % D^6, 2 % D^7.

6,6,5a,9,9-penta-Deutero-2-exo-methoxy-1-methylbicyclo[2.2.2]-octane (81) (21 %): ^1H nmr δ_H ($CDCl_3$) essentially as for the non deuterated compound, except 3.02 had lost the $^4J_{2,6a}$ coupling of 1.7 Hz, H2; 1.85 had lost $^4J_{3endo,5a}$ 2.9 Hz, H3endo; 1.22, lost $^4J_{7endo,6s}$ 1.2 Hz, H7endo; 1.03 (0.21 H), H6a; 0.77 (m) (0.54 H), Me. ^{13}C nmr δ_C ($CDCl_3$) 82.9, C2; 56.4, OMe; 34.5, C3; 32.0 (L.B.), C7; 25.7, C8; 24.8, C4; C1, C6, C5, Me not observed. ^2H nmr δ_D ($CHCl_3$) 1.64, D6s; 1.46 (ca. 0.95 D), D5a; 1.08, D6a; 0.78 (2.43 D), Me.

Reaction of (38) with methanol p-toluenesulphonic acid at room temperature

To a flask containing 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]-oct-6-ene (38) (215 mg), was added a solution of p-toluenesulphonic acid (12 mg) in anhydrous methanol (4 ml). After 3 days stirring at 25°C a sample was removed for glc analysis which revealed the presence of starting material (13 %), 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84a)

(33 %), 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83a) (25 %) and 6-exo-methoxy-2-methyltricylo[3.2.1.$0^{2,7}$]-octane (85a) (28 %). The mixture was diluted with water, extracted with pentane and the combined pentane extracts washed with sodium hydroxide (0.05M). The organic extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure to give a colourless oil (199 mg, 73 %). Separation was achieved by an $AgNO_3$ column

(2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83a) and 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85a) are only partially separated by glc for retention times upwards of 60 minutes).

Silver nitrate (10 %) on Silica (grade 923)

The 10 % silver nitrate on silica (grade 923) was prepared as described by Freeman.[117b] A loading of 530 mg of the crude reaction mixture in pentane (1 ml) was added to 40 ml of the silver nitrate impreganted silica. Elution with pentane gave 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) and 6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85a) of varying purity. Further elution with pentane / ether (50:50) gave 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84a), followed by 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83a).

2-endo-Methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83a): ^1H nmr δ_H ($CDCl_3$) 6.03 (d of d), $^3J_{7,6}$ 5.7 Hz, $^3J_{7,1}$ 2.8 Hz, H7; 5.88 (d of d), $^3J_{6,7}$ 5.8 Hz, $^3J_{6,5}$ 2.7 Hz, H6; 3.20 (s), OMe; 2.59 (d of d), $^3J_{1,7}$ 2.5 Hz, $^3J_{1,8a}$ 5.5 Hz, H1; 2.52 (s), $W_{h/2}$ 10 Hz, H5; 1.87 (m), $^2J_{8s,8a}$ 10.7 Hz, $^3J_{8a,5}$ = $^3J_{8a,1}$ 5.3 Hz, $^4J_{8a,4endo}$ 1.7 Hz, H8a; 1.65 (t of d), $^2J_{3endo,3exo}$ 11.6 Hz, $^3J_{3endo,4endo}$ 3.6 Hz, $^3J_{3endo,4exo}$ 11.6 Hz, H3endo; 1.49 (d), $^2J_{8s,8a}$ 11.0 Hz, H8s;

1.48 (m), H3exo; 1.42 - 1.34 (m), H4exo, H4endo; 1.27 (s), Me. ^{13}C nmr δ_C ($CDCl_3$) 133.8, C7; 133.0, C6; 48.2, OMe; 47.5, C1; 40.7, C8; 39.1, C5; 32.2, C3; 23.0, C4; 21.6, Me; C2 not obs. MS: $C_{10}H_{16}O$ requires $M^{+\cdot}$ 152.1201; Found $M^{+\cdot}$ 152.1195.

2-exo-Methoxy-2-endo-methylbicyclo[3.2.1]octane (84a): ^1H nmr δ_H ($CDCl_3$) 5.94 (d of d), $^3J_{7,1}$ 2.8 Hz, $^3J_{7,6}$ 5.7 Hz, H7; 5.88 (d of d), $^3J_{6,5}$ 2.6 Hz, $^3J_{6,7}$ 5.4 Hz, H6; 3.19, OMe; 2.54, $W_{h/2}$ 15.8 Hz, H1, H5; 1.95 (d), $^2J_{8s,8a}$ 10.0 Hz, H8s; 1.72 (m), $^2J_{8a,8s}$ 10.0 Hz, $^3J_{8a,1} = {}^3J_{8a,5}$ 5.1 Hz, $^4J_{8a,4endo}$ 2.3 Hz, H8a; 1.62 (m), H4exo; 1.55 - 1.50, H3exo, H3endo; 1.23 (m), H4endo; 1.03, Me. ^{13}C nmr δ_C ($CDCl_3$) 135.5, C7; 133.4, C6; 48.8, OMe; 47.5, C1; 38.8, C8; 38.6, C5; 31.2, C3; 23.9, Me; 22.2, C4; C2 not observed. MS: $C_{10}H_{16}O$ requires $M^{+\cdot}$ 152.1201; Found $M^{+\cdot}$ 152.1207.

6-exo-Methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (85a): ^1H nmr δ_H ($CDCl_3$) 3.44 (s), $W_{h/2}$ 2 Hz, H6; 3.33, OMe; 1.98 (s), $W_{h/2}$ 8.8 Hz, H5; 1.82 (m), $^2J_{8a,8s}$ 11.6 Hz, $^3J_{8a,1}$ 3.7 Hz, $^3J_{8a,5}$ 5.6 Hz, $^4J_{8a,4endo}$ 2.1 Hz, H8a; 1.66 - 1.61, H3exo, H3endo; 1.51 (m), H4exo; 1.45 (d), $^2J_{8s,8a}$ 11.7 Hz, H8s; 1.37 (m), H4endo; 1.29, $^3J_{7,1}$ 5.5 Hz, H7; 1.19 (d of d), $^3J_{1,7}$ 5.4 Hz, $^3J_{1,8a}$ 3.8 Hz, H1; 0.92, Me. ^{13}C nmr δ_C ($CDCl_3$) 85.4, C6; 55.6, OMe; 34.9, C5; 29.8, C7; 27.9, C8; 25.7, C4; 25.0, C1; 24.4, Me; 23.3, C3; 21.8, C2. MS: $C_{10}H_{16}O$ requires $M^{+\cdot}$ 152.1201; Found $M^{+\cdot}$ 152.1213. Note: a $Eu(fod)_3$ study was performed on this compound (12.5 mg), $Eu(fod)_3$ being addded incrementally to 13.7 mg total.

Hydrogenation of the products from reaction of (38) and methanol at room temperature

To prehydrogenated palladium on carbon (100 mg, 10 %) in pentane was added a pentane solution of the crude reaction

mixture (140 mg) from the acid catalysed methanol addition of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38). The mixture was shaken under a hydrogen atmosphere for 30 minutes and then the mixture filtered and the solvent removed under reduced pressure to give a colourless oil (80 mg, 57 %). Glc, ^{1}H nmr and ^{13}C nmr showed this to contain mainly 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) and 2-endo-methoxy-2-exo-methyl-bicyclo[3.2.1]octane (72a) in the ratio of 1.37:1 respectively. The data (glc and ^{1}H, ^{13}C nmr) for 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) and 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) are identical with those obtained from the products of reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane (35) with methanol at room temperature as previously described.

Stability of (83b), (84b) and (85b) under the reaction conditions at room temperature

(i) 4-endo-Deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]-oct-6-ene (83b): To a flask containing 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (18 mg, obtained from the acid catalysed reaction of 2-methyl-endo-tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene (38) with methanol-d_1 at room temperature) was added 0.7 ml of a solution containing p-toluenesulphonic acid (493 mg) in anhydrous methanol (25 ml). The flask was stoppered and the contents stirred, a sample being taken for glc analysis every 7 days. Glc analysis showed (83b) did not react to give any other volatile compounds in 21 days.

(ii) 4-endo-Deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]-oct-6-ene (84b): To a flask containing 4-endo-deutero-2-exo-

methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (10 mg, obtained from the acid catalysed reaction of 2-methyl-endo-tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene (38) with methanol-d_1 at room temperature) was added 0.7 ml of a solution containing p-toluenesulphonic acid (493 mg) in anhydrous methanol (25 ml). The flask was stoppered and the contents stirred, a sample being taken for glc analysis every 7 days. After 21 days, the mixture contained 4-endo-deutero-6-exo-methoxy-2-methyl-tricyclo[3.2.1.$0^{2,7}$]octane (85b) and (84b) in the ratio of 1:9.

(iii) 4-endo-Deutero-6-exo-methoxy-2-methyltricyclo-[3.2.1.$0^{2,7}$]octane (85b): To a flask containing 4-endo-deutero-6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]octane (10 mg, obtained from the acid catalysed reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) with methanol-d_1 at room temperature) was added 0.5 ml of a solution containing p-toluenesulphonic acid (94 mg) in anhydrous methanol (25 ml). The flask was stoppered and the contents stirred, a sample being taken for glc analysis every few hours. After 22 hours reaction, the mixture contained 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84b) and (85b) in the ratio of 1:1. This product ratio was invariant for 21 days.

Reaction of (38) with methanol, mercuric acetate

To a stirred solution of 2-methyl-endo-tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene (38) (275 mg) in anhydrous methanol (18 ml) was added mercuric acetate (900 mg). After 2 hours the suspension was filtered to remove unreacted mercuric acetate and the solvent removed under reduced pressure before placing under high vacuum for 12 hours. A pale, viscous oil (840 mg, 89 %) resulted, consisting mainly of 4-endo-acetoxymercurio-

2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83c): ^{1}H nmr δ_H ($CDCl_3$) 6.20 (d of d), $^{3}J_{7,6}$ 5.8 Hz, $^{3}J_{7,1}$ 2.8 Hz, H7; 6.00 (d of d), $^{3}J_{6,7}$ 5.8 Hz, $^{3}J_{6,5}$ 2.6 Hz, H6; 3.19 (s), OMe; 2.90, $W_{h/2}$ 12 Hz, H5; 2.86 (m), $^{3}J_{4exo,3endo}$ 12.5 Hz, $^{3}J_{4exo,3exo}$ 5.5 Hz, $^{3}J_{4exo,5}$ 2.0 Hz, H4exo; 2.56, $W_{h/2}$ 12 Hz, H1; 2.21 (t), $^{2}J_{3endo,3exo}$ 13.0 Hz, $^{3}J_{3endo,4exo}$ 12.9 Hz, H3endo; 2.02 (s), OAc; 1.97 (m), H8a; 1.89 (d of d), $^{2}J_{3exo,3endo}$ 13.0 Hz, $^{3}J_{3exo,4exo}$ 5.5 Hz, H3exo; 1.55 (d), $^{2}J_{8s,8a}$ 9.1 Hz, H8s; 1.29 (s), Me. ^{13}C nmr δ_C ($CDCl_3$) 176.2, OAc; 135.3, $J_{^{199}Hg,^{13}C}$ not obs., C7; 132.7, $J_{^{199}Hg,^{13}C}$ 34 Hz, C6; 77.2, C2; 48.3, OMe; 47.6, $J_{^{199}Hg,^{13}C}$ 25 Hz, C1; 45.1, $J_{^{199}Hg,^{13}C5}$ 74 Hz, C5; 42.7, $J_{^{199}Hg,^{13}C}$ 1640.9 Hz, C4; 41.8, $J_{^{199}Hg,^{13}C}$ 299 Hz, C8; 38.7, $J_{^{199}Hg,^{13}C}$ 64 Hz, C3.

Reduction of the organomercurial mixture with sodium mercury amalgam

Reduction of the organomercurial mixture (477 mg) in sodium deuteroxide was carried out as previously described for the reduction of 4-endo-acetoxymercurio-2-endo-methoxybicyclo-[3.2.1]octane (40c). Isolation gave an oil (150 mg, 85 %), shown to contain 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (84b) (11 %), 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83b) (82 %) and 4-endo-deutero-6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]-octane (85b) (7 %). 4-endo-Deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83b) was separated by preparative glc: ^{1}H nmr δ_H ($CDCl_3$) 6.03 (d of d), $^{3}J_{7,6}$ 5.7 Hz, $^{3}J_{7,1}$ 2.8 Hz, H7; 5.88 (d of d), $^{3}J_{6,7}$ 5.8 Hz, $^{3}J_{6,5}$ 2.7 Hz, H6; 3.20 (s), OMe; 2.59 (d of d), $^{3}J_{1,7}$ 2.5 Hz, $^{3}J_{1,8a}$ 5.9 Hz, H1; 2.52 (d of t), $^{3}J_{5,4exo} = {}^{3}J_{5,6}$ 2.5 Hz, $^{3}J_{5,8a}$ 5.3 Hz, H5; 1.87 (d of t), $^{2}J_{8s,8a}$ 10.6 Hz, $^{3}J_{8a,5}$ =

$^{3}J_{8a,1}$ 5.3 Hz, H8a; 1.65 (t), $^{2}J_{3\underline{endo},3\underline{exo}}$ = $^{3}J_{3\underline{endo},4\underline{exo}}$ 12.5 Hz, H3endo; 1.49 (d), $^{2}J_{8s,8a}$ 11.4 Hz, H8s; 1.48 (m), H3exo; 1.42 - 1.34 (m), H4exo; 1.27 (s), Me. ^{13}C nmr δ_C ($CDCl_3$) 133.8, C7; 133.0, C6; Approx. 77, C2; 48.2, OMe; 47.5, C1; 40.7 (L.B.), C8; 39.0 (L.B.), C5; 32.1 (L.B.), C3; 22.6, $J_{^{13}C,^{2}H}$ 19.8 Hz, C4; 21.5, Me. Nb: (L.B.) indicates the presence of a small $^{13}C,^{2}H$ coupling. ^{2}H nmr δ_D ($CHCl_3$) 1.35, D4endo.

Hydrogenation of the reduction products from the sodium mercury amalgam reduction in sodium hydroxide

To prehydrogenated palladium on carbon (10 %, 100 mg) in pentane was added the products from the sodium mercury reduction in sodium hydroxide (225 mg). The mixture was shaken under a hydrogen atmosphere for 1 hour, filtered and the solvent removed under reduced pressure to give an oil (164 mg, 73 %) shown by glc analysis and ^{13}C nmr to contain 2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (73a) (10 %), unknown compounds (12 %) and 2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (72a) (78 %). The data (glc and ^{13}C nmr) are identical with those from the products from reaction of 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]octane with methanol at room temperature.

Reaction of (38) with methanol-d_1, p-toluenesulphonic acid at room temperature

The acid catalysed methanol-d_1 addition to 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) (845 mg) was carried out as described for the reaction with methanol at room temperature. Reaction for 7 days and subsequent isolation gave a colourless oil (854 mg, 79 %), subsequently shown by glc

analysis to contain 2-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (38) (21 %), presumably deutero-2-methylbicyclo[3.2.1]-octa-2,6-diene (7 %), 4-endo-deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]octane (84b) (30 %), 4-endo-deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]octane (83b) (17 %) and 4-endo-deutero-6-exo-methoxy-2-methyl-tricyclo[3.2.1.$0^{2,7}$]octane (85b) (17 %). Separation was effected on a silver nitrate impregnated silica column as previously described in the acid catalysed reaction with methanol at room temperature.

4-endo-Deutero-2-endo-methoxy-2-exo-methylbicyclo[3.2.1]oct-6-ene (83b): The spectral data are presented in the sodium mercury amalgam reduction in sodium deuteroxide of the crude organomercurial mixture. Mass spectrum shows 2 % D^0, 95 % D^1, 3 % D^2.

4-endo-Deutero-2-exo-methoxy-2-endo-methylbicyclo[3.2.1]oct-6-ene (84b): ^{1}H nmr δ_H ($CDCl_3$) 5.94 (d of d), $^3J_{7,1}$ 2.8 Hz, $^3J_{7,6}$ 5.7 Hz, H7; 5.88 (d of d), $^3J_{6,5}$ 2.6 Hz, $^3J_{6,7}$ 5.4 Hz, H6; 3.19, OMe; 2.54, $W_{h/2}$ 12.4 Hz, H1, H5; 1.95 (d), $^2J_{8s,8a}$ 10.0 Hz, H8s; 1.72 (d of t), $^2J_{8a,8s}$ 10.0 Hz, $^3J_{8a,1} = {}^3J_{8a,5}$ 5.1 Hz, H8a; 1.62 (m), H4exo; 1.55 - 1.50, H3exo, H3endo; 1.03, Me. ^{13}C nmr δ_C ($CDCl_3$) 135.4, C7; 133.3, C6; 48.8, OMe; 47.5 (L.B.), C1; 38.8 (L.B.), C8; 38.5 (L.B.), C5; 31.0, C3; 23.8, Me; 21.7, $J_{^{13}C,^2H}$ 19.6 Hz, C4; C2 not observed. ^{2}H nmr δ_D ($CHCl_3$) 1.22, H4endo. Mass spectrum shows 1 % D^0, 98 % D^1, 1 % D^2.

4-endo-Deutero-6-exo-methoxy-2-methyltricyclo[3.2.1.$0^{2,7}$]-octane (85b): ^{1}H nmr δ_H ($CDCl_3$) 3.44 (s), $W_{h/2}$ 2 Hz, H6; 3.33, OMe; 1.94 (d of d), $^3J_{5,4exo}$ 4.6 Hz, $^3J_{5,8a}$ 5.2 Hz, H5; 1.82 (m), $^2J_{8a,8s}$ 11.6 Hz, $^3J_{8a,1}$ 3.7 Hz, $^3J_{8a,5}$ 5.6 Hz, H8a; 1.66 - 1.61, H3exo, H3endo; 1.51 (br. d), $^3J_{4exo,3exo}$ ca.

12 Hz, H4exo; 1.45 (d), $^{2}J_{8s,8a}$ 11.6 Hz, H8s; 1.29 (d), $^{3}J_{7,1}$ 5.6 Hz, H7; 1.18 (d of d), $^{3}J_{1,7}$ 5.5 Hz, $^{3}J_{1,8a}$ 3.8 Hz, H1; 0.91, Me. ^{13}C nmr δ_C ($CDCl_3$) 85.3, C6; 55.6, OMe; 34.8 (L.B.), C5; 29.8, C7; 27.8 (L.B.), C8; 25.4, $J_{^{13}C,^{2}H}$ 19.3 Hz, C4; 25.0, C1; 24.4, Me; 23.2, C3; 21.8, C2. ^{2}H nmr δ_D ($CHCl_3$) 1.32, D4endo. Mass spectrum shows 6 % D^0, 92 % D^1, 2 % D^2.

Reaction of (39) with bromine in CCl_4

To a stirred solution of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (220 mg) in CCl_4 (10 ml) was added bromine (292 mg, 0.88 molar equivalent) in CCl_4 (5 ml). The mixture was stirred for 3 minutes before removal of the solvent and unreacted starting material under reduced pressure to give a pale yellow oil (466 mg, 96 %). Separation was effected by radial chromatography (SiO_2, pentane) to give 6-exo-bromotricyclo[3.2.1.$0^{2,7}$]-oct-3-ene (94) (19 %), 6-endo-7-exo-dibromo-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (92) (6 %), 4-exo-6-exo-dibromo-tricyclo[3.2.1.$0^{2,7}$]octane (95a) (39 %), 5-exo-bromo-3-exo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (93a) (30 %) and 6-exo-7-exo-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (91) (6 %).

6-exo-Bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene (94): ^{1}H nmr δ_H ($CDCl_3$) 5.87-5.80 (m), H3, H4; 3.64 (s), $W_{h/2}$ 2 Hz, H6; 2.75 (t), $^{3}J_{5,8a}$ 6.0 Hz, $^{3}J_{4,5}$ 6.5 Hz, H5; 2.25 (m), $^{2}J_{8a,8s}$ 11.8 Hz, $^{3}J_{8a,1}$ 2.4 Hz, $^{3}J_{8a,5}$ 6.0 Hz, H8a; 1.74 (s), $W_{h/2}$ 9 Hz, H2, H7; 1.68 (t of d), $^{3}J_{1,2} = {}^{3}J_{1,7}$ 6.0 Hz, $^{4}J_{1,5}$ 1.8 Hz, H1; 0.88 (d), $^{2}J_{8a,8s}$ 11.8 Hz, H8s. The ^{1}H nmr of this compound has previously been reported.[106] ^{13}C nmr δ_C ($CDCl_3$) 127.1, C4; 123.0, C3; 56.2, C6; 42.0, C5; 25.4, C8; 22.1, C7; 20.0, C2; 15.1, C1.

6-endo-7-exo-Dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (92): ^{1}H nmr δ_H ($CDCl_3$) 4.38 (t), $^{3}J_{5,6} = {}^{3}J_{6,7}$ 3.2 Hz, H6; 3.93 (t), $^{3}J_{7,6} = {}^{4}J_{7,8s}$ 3.2 Hz, H7; 2.57 (s), $W_{h/2}$ 3.8 Hz, H1; 2.54 (s), $W_{h/2}$ 10 Hz, H5; 1.42 (d of t), $^{2}J_{8a,8s}$ 11.8 Hz, $^{4}J_{8a,2} = {}^{4}J_{8a,4}$ 1.3 Hz, H8a; 1.12 (d of d), $^{2}J_{8a,8s}$ 11.8 Hz, $^{4}J_{7,8s}$ 3.2 Hz, H8s; 0.92, H2,4; 0.67 (d of t), $^{2}J_{3exo,3endo}$ 6.3 Hz, $^{3}J_{3exo,2} = {}^{3}J_{3exo,4}$ 3.2 Hz, H3exo; 0.32 (m), $^{2}J_{3endo,3exo}$ 6.3 Hz, $^{3}J_{3endo,2} = {}^{3}J_{3endo,4}$ 7.1 Hz, H3endo. ^{13}C nmr δ_C ($CDCl_3$) 63.0, C6; 59.5, C7; 47.1, C1; 43.9, C5; 24.6, C8; 13.8, 11.2, C2, C4; 4.22, C3.

4-exo-6-exo-Dibromotricyclo[3.2.1.$0^{2,7}$]octane (95a): ^{1}H nmr δ_H ($CDCl_3$) 4.30 (s), $W_{h/2}$ 3 Hz, H6endo; 4.14 (m), $^{3}J_{4endo,3exo} = {}^{3}J_{4endo,3endo}$ 7.0 Hz, $^{3}J_{4endo,5} = {}^{4}J_{4endo,8a}$ 1.6 Hz, H4endo; 2.55 (s), $W_{h/2}$ 6 Hz, H5; 2.52 (m), $^{2}J_{3exo,3endo}$ 15.5 Hz, $^{3}J_{3endo,2}$ 3.4 Hz, $^{3}J_{4endo,3endo}$ 7.0 Hz, H3endo; 2.39 (m), $^{2}J_{3exo,3endo}$ 15.5 Hz, $^{3}J_{3exo,2}$ 1.9 Hz, $^{3}J_{3exo,4endo}$ 7.0 Hz, H3exo; 2.20 (s), $W_{h/2}$ 5 Hz, H8s,8a; 1.85 (m), $^{3}J_{7,1} = {}^{3}J_{7,2}$ 6.6 Hz, $^{4}J_{7,5} = {}^{4}J_{7,8s}$ 1.3 Hz, H7; 1.67 (s), $W_{h/2}$ 11 Hz, H1; 1.00 (m), $^{3}J_{2,1} = {}^{3}J_{2,7}$ 7.0 Hz, $^{3}J_{2,3endo}$ 3.4 Hz, $^{3}J_{2,3exo}$ 1.9 Hz, H2. ^{13}C nmr δ_C ($CDCl_3$) 55.2, C6; 49.8, C5; 47.8, C4; 29.6, C3; 25.3, C7; 23.0, C8; 18.4, C2; 18.0, C1. MS: $C_8H_{10}Br_2$ requires $M^{+\cdot}$ 267.9111; Found $M^{+\cdot}$ 267.9110.

5-exo-Bromo-3-exo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (93a): ^{1}H nmr δ_H ($CDCl_3$) 3.96 (s) $W_{h/2}$ 3.2 Hz, H5; 3.28 (d of d), $^{2}J_{8a,8b}$ 10.1 Hz, $^{3}J_{8a,3}$ 7.2 Hz, H8a; 3.18 (d of d), $^{2}J_{8b,8a}$ 10.1 Hz, $^{3}J_{8b,3}$ 8.7 Hz, H8b; 2.22 (s), $W_{h/2}$ 5 Hz, H4; 2.12 (d of d), $^{3}J_{3,8a}$ 7.2 Hz, $^{3}J_{3,8b}$ 8.7 Hz, H3; 2.05 (d), $^{2}J_{7a,7s}$ 11.8 Hz, H7a; 1.67 (t), $^{3}J_{6,1} = {}^{3}J_{6,2}$ 5.2 Hz, H6; 1.52 (d), $^{2}J_{7a,7s}$ 11.8 Hz, H7s; 1.44 (t), $^{3}J_{1,2} = {}^{3}J_{1,6}$ 5.0 Hz, H1; 1.30 (t), $^{3}J_{2,1} = {}^{3}J_{2,6}$ 5.0 Hz, H2. ^{13}C

nmr δ_C ($CDCl_3$) 55.9, C5; 46.1, C3; 40.9, C4; 32.4, C8; 27.0, C7; 20.8, C6; 18.8, C2; 11.7, C1. MS: $C_8H_{10}Br_2$ requires $M^{+\cdot}$ 267.9111; Found $M^{+\cdot}$ 267.9100.

6-exo-7-exo-Dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (91): ^1H nmr δ_H ($CDCl_3$) 4.21 (d), $^4J_{6endo/7endo}$, 8s 2.3 Hz, H6endo, H7endo; 2.63 (s), $W_{h/2}$ 3 Hz, H1, H5; 1.65 (d), $^2J_{8a,8s}$ 11.8 Hz, H8a; 1.06 (d of t), $^2J_{8a,8s}$ 11.8 Hz, $^4J_{8s,6endo} = {}^4J_{8s,7endo}$ 2.3 Hz, H8s; 0.88 (d of d), $^3J_{2/4,3exo}$ = 3.0 Hz, $^3J_{2/4,3endo}$ = 7.0 Hz, H2,4; 0.72 (d of t), $^2J_{3exo,3endo}$ 6.3 Hz, $^3J_{2,3exo} = {}^3J_{4,3exo}$ 3.0 Hz, H3exo; 0.38 (m), $^2J_{3exo,3endo}$ 6.3 Hz, $^3J_{2,3endo} = {}^3J_{4,3endo}$ 7.0 Hz, H3endo. ^{13}C nmr δ_C ($CDCl_3$) 56.7, C6,7; 47.8, C1,5; 22.4, C8; 14.8, C2,4; 6.1, C3.

Reaction of (39) with bromine in methanol

To a solution of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) (170 mg) in anhydrous methanol (15 ml) was added bromine (225 mg, 0.88 molar equivalent) in methanol (2 ml). The mixture was stirred for 2 minutes and then CCl_4 (5 ml) added. The mixture was washed with water, the organic layer separated, dried over $MgSO_4$ and the solvent removed under reduced pressure to give a clear, colourless oil (268 mg, 84 %), shown to contain 4-exo-6-exo-dibromotricyclo[3.2.1.$0^{2,7}$]octane (95a) (11 %), 5-exo-bromo-3-exo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (93a) (11 %) 6-exo-bromo-4exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (95b) (39 %) and 5-exo-bromo-3-exo-methoxymethyl-tricyclo[2.2.1.$0^{2,6}$]heptane (93b) (29 %). Separation was effected by radial chromatography (SiO_2, petroleum ether). The spectral data for 4-exo-6-exo-dibromotricyclo[3.2.1.$0^{2,7}$]octane (95a) and 5-exo-bromo-3-exo-bromomethyltricyclo-

[2.2.1.$0^{2,6}$]heptane (93a) are identical to those reported for the reaction of exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39) with bromine in CCl_4 previously.

6-exo-Bromo-4-exo-methoxytricyclo[3.2.1.$0^{2,7}$]octane (95b): ^1H nmr δ_H ($CDCl_3$) 4.22 (s), $W_{h/2}$ 3 Hz, H6endo; 3.27 (m), H4; 3.23, OMe; 2.44 (t), $^3J_{5,8} = {}^3J_{5,4}$ 3.2 Hz, H5; 2.15 (m), $^2J_{3endo,3exo}$ 14.9 Hz, $^3J_{3endo,2}$ 3.5 Hz, $^3J_{3endo,4}$ 9.5 Hz, H3endo; 1.95, H8a,8s; 1.77 (t of t), $^3J_{7,1}$ 7.5 Hz, $^3J_{7,2}$ 6.8 Hz, $^4J_{7,5} = {}^4J_{7,8s}$ 1.1 Hz, H7; 1.67 (m), $^2J_{3exo,3endo}$ 14.7 Hz, $^3J_{3exo,2}$ 2.1 Hz, $^3J_{3exo,4}$ 4.8 Hz, H3exo; 1.60 (s), $W_{h/2}$ 14 Hz, H1; 0.95 (m), $^3J_{2,1} = {}^3J_{2,7}$ 7.5 Hz, $^3J_{2,3exo}$ 2.1 Hz, $^3J_{2,3endo}$ 3.5 Hz, H2. ^{13}C nmr δ_C ($CDCl_3$) 77.5, C4; 56.3, C6; 55.8, OMe; 44.5, C5; 25.7, C7; 25.0, C3; 21.0, C8; 18.1, C1; 16.1, C2. MS: $C_9H_{13}OBr$ requires $M^{+\cdot}$ 216.0150; Found $M^{+\cdot}$ 216.0149.

5-exo-Bromo-3-exo-methoxymethyltricyclo[2.2.1.$0^{2,6}$]heptane (93b): ^1H nmr δ_H ($CDCl_3$) 3.95 (s), $W_{h/2}$ 3.3 Hz, H5; 3.32, OMe; 3.26 (d of d), $^2J_{8a,8b}$ 11.7 Hz, $^3J_{8a,3}$ 8.6 Hz, H8a; 3.21 (d of d), $^2J_{8b,8a}$ 11.7 Hz, $^3J_{8b,3}$ 9.5 Hz, H8b; 2.13 (s), $W_{h/2}$ 5 Hz, H4; 1.95 (d of t), $^2J_{7a,7s}$ 11.5 Hz, $^4J_{7a,3} = {}^4J_{7a,4}$ 1.5 Hz, H7a; 1.92 (t), $^3J_{3,8a}$ 8.6 Hz, $^3J_{3,8b}$ 9.5 Hz, H3; 1.55 (t), $^3J_{6,1} = {}^3J_{6,2}$ 5.3 Hz, H6; 1.53 (d), $^2J_{7s,7a}$ 11.6 Hz, H7s; 1.38 (t), $^3J_{1,2} = {}^3J_{1,6}$ 5.0 Hz, H1; 1.19 (t), $^3J_{2,1} = {}^3J_{2,6}$ 5.2 Hz, H2. ^{13}C nmr δ_C ($CDCl_3$) 72.4, C8; 59.0, OMe; 57.0, C5; 43.3, C3; 39.2, C4; 27.3, C7; 19.6, C6; 16.7, C2; 11.7, C1. MS: $C_9H_{13}OBr$ requires $M^{+\cdot}$ 216.0150; Found $M^{+\cdot}$ 216.0146.

Reaction of (37) with bromine in CCl_4

To a solution of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) (83 mg) in CCl_4 (15 ml) was added with stirring bromine (122

mg, 0.97 molar equivalent). After 2 minutes the solvent was removed under reduced pressure to yield a yellowish oil (183 mg, 88 %). Glc analysis showed five products, later shown to be 5-exo-bromo-3-endo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (101a) (59 %), 6-exo-8-anti-dibromo-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (102a) (22 %) and 3 unknown compounds (5 %, 6 % and 7 %). Separation was achieved by careful radial chromatography (SiO_2, pet. ether).

5-exo-Bromo-3-endo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (101a): ^{1}H nmr δ_H ($CDCl_3$) 4.04 (s), $W_{h/2}$ 2.5 Hz, H5; 3.23 (d of d), $^2J_{8a,8b}$ 10.2 Hz, $^3J_{8a,3}$ 7.7 Hz, H8a; 3.12 (d of d), $^2J_{8a,8b}$ 10.2 Hz, $^3J_{8b,3}$ 8.7 Hz, H8b; 2.12-2.16, H4, H7a; 2.04 (t), $^3J_{8a,3}$ 7.7 Hz, $^3J_{8b,3}$ 8.7 Hz, H3; 1.62-1.53, H6, H1; 1.38 (d), $^2J_{7s,7a}$ 10.8 Hz, H7s; 1.23 (t), $^3J_{2,1} = {}^3J_{2,6}$ 5.0 Hz, H2. ^{13}C nmr δ_C ($CDCl_3$) 53.6, C5; 48.1, C3; 40.8, C4; 32.6, C7; 32.5, C8; 19.3, C2; 18.3, C6; 14.4, C1. M.S.: $C_8H_{10}Br_2$ requires $M^{+\cdot}$ 263.9150; Found $M^{+\cdot}$ 263.9140.

6-exo-8-anti-Dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102a): ^{1}H nmr δ_H ($CDCl_3$) 3.98 (m), $^3J_{6endo,7endo}$ 8.0 Hz, $^3J_{6endo,7exo}$ 4.5 Hz, $^4J_{6endo,8}$ 1.5 Hz, H6endo; 3.78 (m), $^3J_{8s,1} = {}^3J_{8s,5} = {}^4J_{8s,6endo} = {}^4J_{8s,7endo}$ 1.6 Hz, H8s; 2.79 (t), $^4J_{5,1} = {}^4J_{5,2}$ 1.5 Hz, H5; 2.58 (m), $^2J_{7exo,7endo}$ 13.4 Hz, $^3J_{7exo,6endo}$ 4.5 Hz, $^3J_{7exo,1}$ 3.3 Hz, H7exo; 2.50 (s), $W_{h/2}$ 8 Hz, H1; 2.33 (m), $^2J_{7exo,7endo}$ 13.4 Hz, $^3J_{6endo,7endo}$ 8.0 Hz, $^4J_{8syn,7endo}$ 1.8 Hz, H7endo; 0.98 (m), $^3J_{2,3endo} = {}^3J_{2,4}$ 7.3 Hz, $^3J_{2,3exo}$ 3.3 Hz, $^4J_{2,5}$ 1.5 Hz, H2; 0.88 (t of d), $^3J_{4,3exo}$ 3.2 Hz, $^3J_{4,3endo} = {}^3J_{4,2}$ 7.3 Hz, H4; 0.78 (m), $^2J_{3exo,3endo}$ 7.0 Hz, $^3J_{3exo,2} = {}^3J_{3exo,4}$ 3.2 Hz, H3exo; 0.27 (m), $^2J_{3endo,3exo}$ 7.0 Hz, $^3J_{3endo,2}$ 7.2 Hz, $^3J_{3endo,4}$ 7.3 Hz, H3endo. ^{13}C nmr δ_C ($CDCl_3$) 48.7, C5; 47.9,

C6; 47.7, C8; 44.4, C1; 41.8, C7; 16.4, C4; 15.2, C2; 4.8, C3. M.S.: $C_8H_{10}Br_2$ requires $M^{+\cdot}$ 263.9150; Found $M^{+\cdot}$ 263.9149.

Reaction of (37) with bromine in methanol

To a stirred solution of endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (37) (240 mg) in anhydrous methanol (15 ml) was added bromine (360 mg, 0.99 molar equivalent) in methanol (1 ml). After 2 minutes, CCl_4 (5 ml) was added, the mixture washed with water and the organic layer separated. The extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure to give a clear, colourless oil (503 mg, 98 %) shown to contain 5-exo-bromo-3-endo-bromomethyl-tricyclo[2.2.1.$0^{2,6}$]heptane (101a) (17 %), 6-exo,8-anti-dibromo-exo-tricyclo-[3.2.1.$0^{2,4}$]octane (102a) (4 %), 5-exo-bromo-3-endo-methoxymethyltricyclo[2.2.1.$0^{2,6}$]heptane (101b) (31 %) and 8-anti-bromo-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102b) (37 %). Separation was effected by radial chromatography (SiO_2, eluted first with petroleum ether to give the dibromides and then 5 % ether/petroleum ether to give the bromo-methoxy ethers). The spectral data for 5-exo-bromo-3-endo-bromomethyltricyclo[2.2.1.$0^{2,6}$]heptane (101a) and 6-exo,8-anti-dibromo-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102a) are identical to those reported for the reaction of endo-tricyclo[3.2.1.$0^{2,4}$]octane (37) with bromine in CCl_4 previously.

8-anti-Bromo-6-exo-methoxy-exo-tricyclo[3.2.1.$0^{2,4}$]octane (102b): ^{1}H nmr δ_H ($CDCl_3$) 3.68 (s), $W_{h/2}$ 5 Hz, H8s; 3.55 (m), $^3J_{6endo,7endo}$ 6.4 Hz, $^3J_{6endo,7exo}$ 3.7 Hz, $^4J_{6endo,8s}$ 1.6 Hz, H6; 3.33, OMe; 2.67 (s), $W_{h/2}$ 5 Hz, H5; 2.42 (s), $W_{h/2}$ 7 Hz, H1; 2.08 (m), $^2J_{7exo,7endo}$ 12.6 Hz, $^3J_{7exo,1} = {}^3J_{7exo,6endo}$ 3.7 Hz, H7exo; 1.98 (d of d),

$^{2}J_{7\underline{endo},7\underline{exo}}$ 12.6 Hz, $^{3}J_{7\underline{endo},6\underline{endo}}$ 6.4 Hz, H7<u>endo</u>; 0.90 (m), $^{3}J_{2,5}$ 1.4 Hz, $^{3}J_{2,3\underline{exo}}$ 3.2 Hz, $^{3}J_{2,3\underline{endo}} = {}^{3}J_{2,4}$ 7.4 Hz, H2; 0.76 (d of t), $^{2}J_{3\underline{exo},3\underline{endo}}$ 7.2 Hz, $^{3}J_{3\underline{exo},4} = {}^{3}J_{3\underline{exo},2}$ 3.2 Hz, H3<u>exo</u>; 0.62 (t of d), $^{3}J_{4,2} = {}^{3}J_{4,3\underline{endo}}$ 7.2 Hz, $^{3}J_{4,3\underline{exo}}$ 3.2 Hz, H4; 0.25 (m), $^{2}J_{3\underline{endo},3\underline{exo}} = {}^{3}J_{3\underline{endo},2} = {}^{3}J_{3\underline{endo},4}$ 7.2 Hz, H3<u>endo</u>. ^{13}C nmr δ_C ($CDCl_3$) 84.9, C6; 56.8, OMe; 48.4, C8; 43.8, C1; 42.3, C5; 38.4, C7; 16.1, C4; 14.0, C2; 5.3, C3. M.S.: $C_9H_{13}OBr$ requires $M^{+\cdot}$ 216.0150; Found $M^{+\cdot}$ 216.0146.

5-<u>exo</u>-Bromo-3-<u>endo</u>-methoxymethyltricyclo[2.2.1.$0^{2,6}$]heptane (101b): ^{1}H nmr δ_H ($CDCl_3$) 4.22 (s), $W_{h/2}$ 4 Hz, H5; 3.32, OMe; 3.29 (d of d), $^{2}J_{8a,8b}$ 10.1 Hz, $^{3}J_{8b,3}$ 8.1 Hz, H8a; 3.25 (d of d), $^{2}J_{8a,8b}$ 10.1 Hz, $^{3}J_{8b,3}$ 9.6 Hz, H8b; 2.15-2.10, H7a, H4; 1.96 (t), $^{3}J_{8b,3}$ 8.1 Hz, $^{3}J_{8b,3}$ 9.6 Hz, H3; 1.52 (t), $^{3}J_{6,1} = {}^{3}J_{6,2}$ 5.2 Hz, H6; 1.44 (t), $^{3}J_{1,2} = {}^{3}J_{1,6}$ 5.0 Hz, H1; 1.42 (d), $^{2}J_{7a,7s}$ 10.8 Hz, H7s; 1.20 (t), $^{3}J_{2,1} = {}^{3}J_{2,6}$ 5.1 Hz, H2. ^{13}C nmr δ_C ($CDCl_3$) 72.3, C8; 59.0, OMe; 55.4, C5; 45.3, C3; 39.1, C4; 32.5, C7; 18.4, C6; 17.0, C2; 13.1, C1. M.S.: $C_9H_{13}OBr$ requires $M^{+\cdot}$ 216.0150; Found $M^{+\cdot}$ 216.0146.

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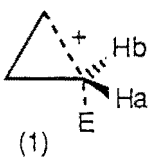
Acknowledgements

I wish to express my thanks to Drs. J.M. Coxon and P.J. Steel for their expert supervision of my research and to Professor M.A. Battiste for his enlightening discussions.

I would also like to thank the academic and technical staff of the Chemistry Department of the University of Canterbury for their assistance.

The award of a University Grants Committee postgraduate scholarship is gratefully acknowledged.

Finally, I would like to extend a special word of thanks to my family and friends for their support and encouragement.



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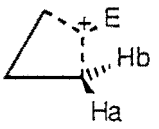

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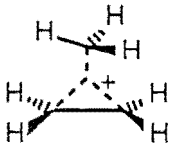
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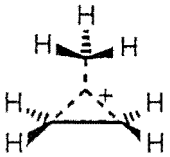
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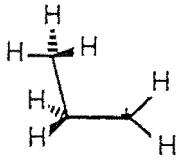
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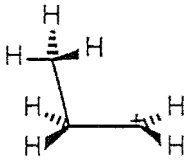
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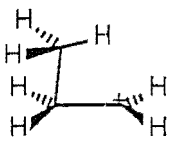
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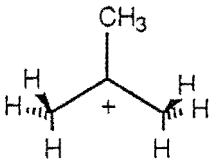

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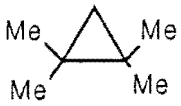

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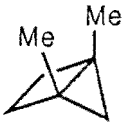

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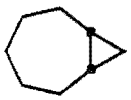
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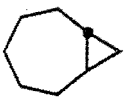
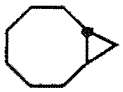

(20)


(21)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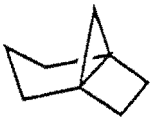
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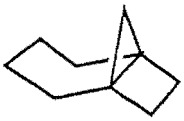
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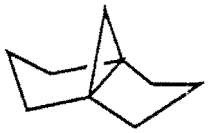
(25)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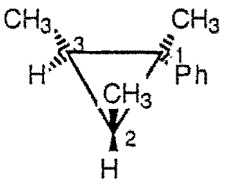

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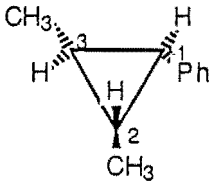

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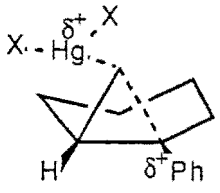

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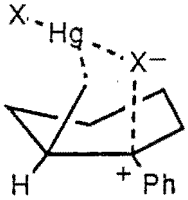

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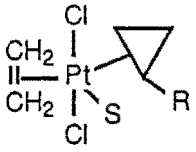

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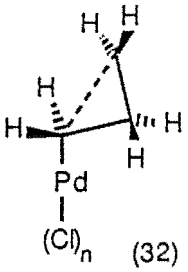

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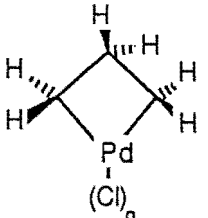

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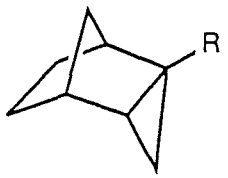
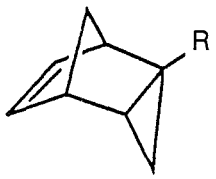


(34) R = H

(35) R = Me

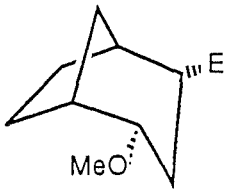
(36)



(37) R = H

(38) R = Me

(39)



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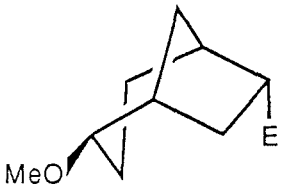

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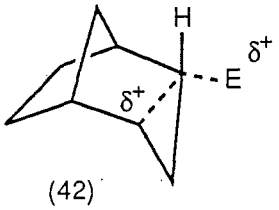

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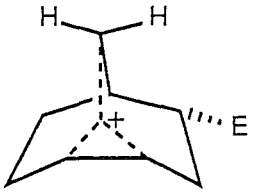

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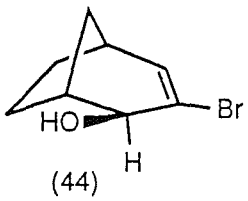

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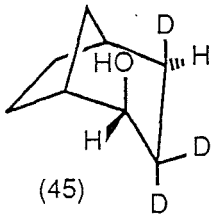

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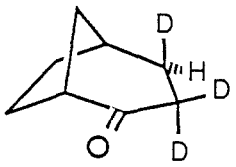

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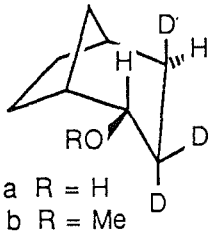
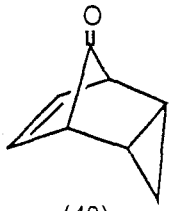


(47) a R = H
b R = Me



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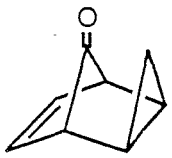

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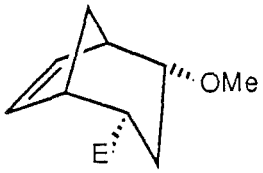

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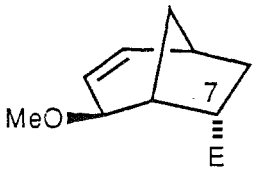

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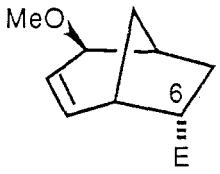

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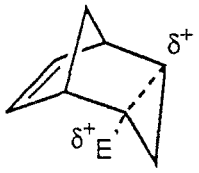

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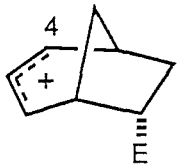

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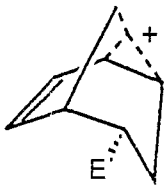

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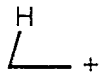

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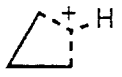
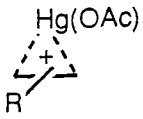


(57)

(58)



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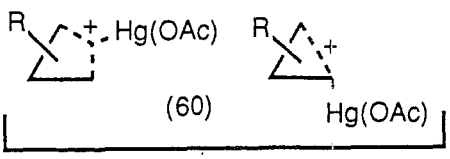
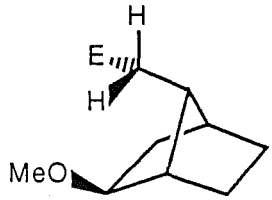


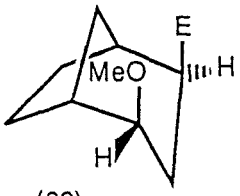
(60)

For compounds (40) to (88)

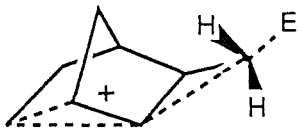
(a) E = H
(b) E = D
(c) E = HgOAc
(d) E = HgSCN



(61)



(62)



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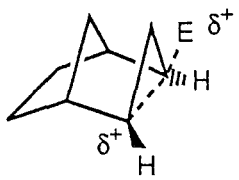
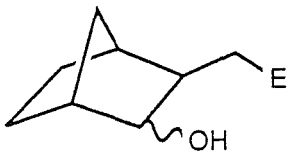


(64)



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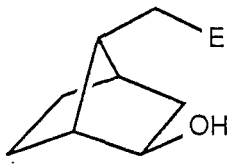

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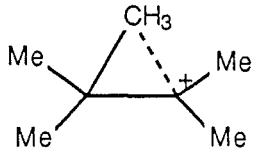

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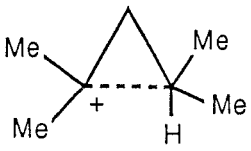
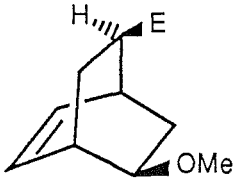


(68)

(69)



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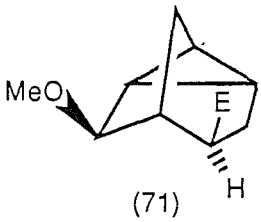

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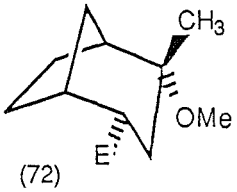

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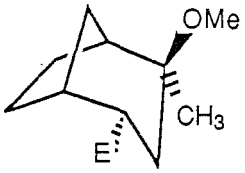
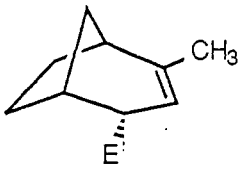
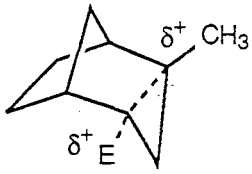


(73)



(74)



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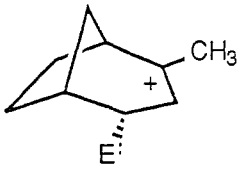
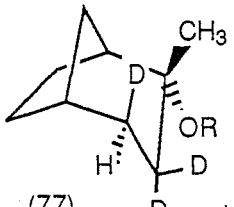
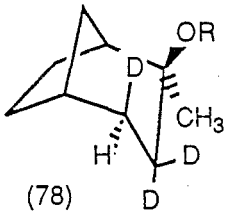


(76)



(77)

a) R = H
b) R = Me



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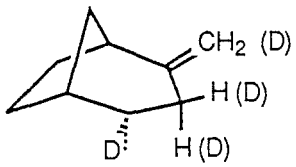

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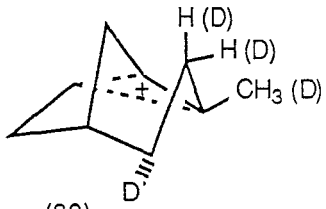

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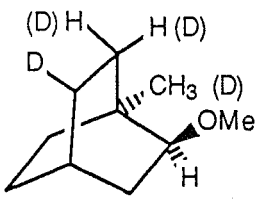

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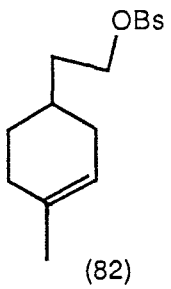

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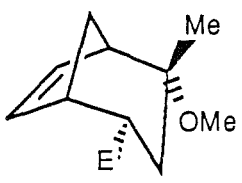

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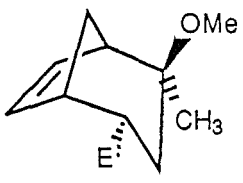

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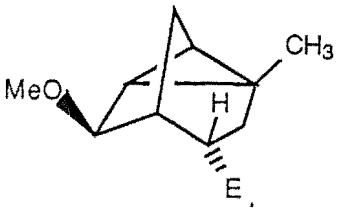

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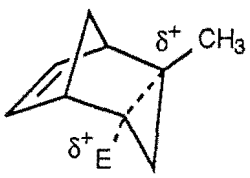

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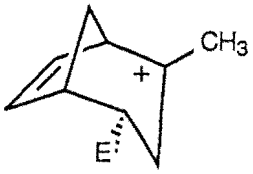

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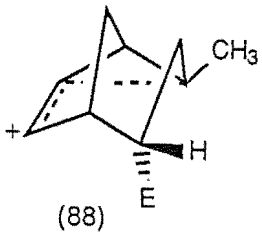

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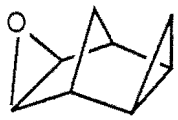

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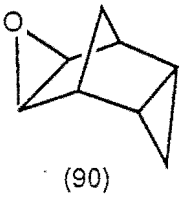

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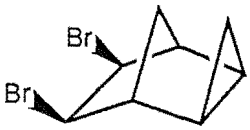

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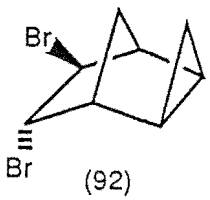

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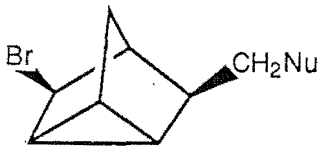

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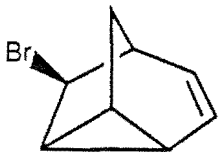

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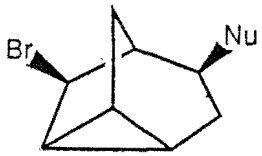

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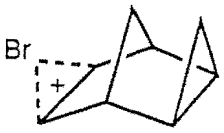

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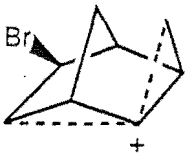

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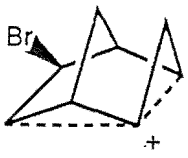

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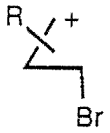

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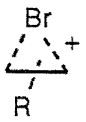

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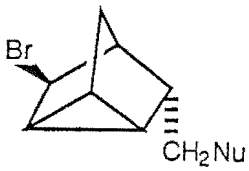

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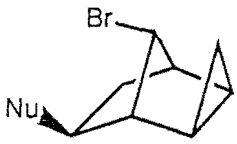

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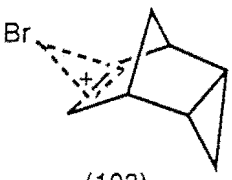

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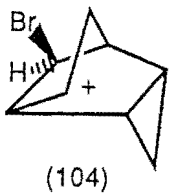

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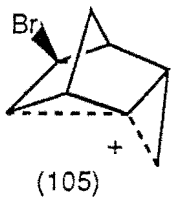

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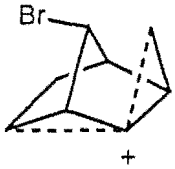

(106)

For compounds (93), (95), (101), (102)
Nu = a) Br
b) MeO